Ministry of Environment and Food of Denmark
Environmental Protection Agency

Exposure of children and unborn children to selected chemical substances

Survey of chemical substances in consumer products No. 158
April 2017

Publisher: Danish Environmental Protection Agency

Editors:
Poul Bo Larsen, DHI
Julie Boberg, DTU Food
Pia Brunn Poulsen, Force
Thit Aarøe Mørck, DHI
Helle Buchardt Boyd, DHI
Dorthe Nørgaard Andersen, DHI
Marta Axelstad, DTU Food
Ulla Hass, DTU Food

ISBN: 978-87-93529-84-7

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Foreword

This project is part of the wish of the government and “Enhedslisten” to safeguard children and young people from harmful and unnecessary chemistry. This project focuses on the existing knowledge of exposure of children and unborn children to endocrine disrupting substances (including suspected endocrine disrupting substances) and/or substances that are harmful to the nervous system. The objective is to establish whether individual sources that pose a risk to children and pregnant women/ unborn children can be identified, or whether the total exposure to substances with identical effects from multiple sources may cause a risk. At the same time, it is the intention that the project should benefit from the large amount of data obtained from the studies conducted under the Environmental Protection Agency's child chemistry package.

The project was carried out between March 2016 and December 2016 in collaboration between DHI and the DTU Food Institute.

A working group has been assigned to the project, consisting of:

Shima Dobel, Danish EPA (project responsible)
Bettina Ørsnes Larsen, Danish EPA (project responsible)
Marie Louise Holmer, Danish EPA
Charlotte Legind, Danish Veterinary and Food Administration
Mette Holm, Danish Veterinary and Food Administration
Julie Boberg, DTU Food
Pia Brunn Poulsen, Force
Poul Bo Larsen, DHI (project manager)

Summary and conclusion

Objective and starting point

The overall objective of this project is to assess whether there may be a risk of the overall exposure of children under 3 years and pregnant women/ unborn children to endocrine disrupting substances (including suspected endocrine disrupting substances) and chronic neurotoxic substances. The project was implemented in the following steps:

- Identification of endocrine disrupting, suspected endocrine disrupting and chronic neurotoxic substances to which children under 3 years and pregnant women/ unborn children may be potentially exposed.
- Collection of relevant literature to assess the exposure to the substances, including relevant biomonitoring data.
- Description of exposure/ exposure scenarios for the individual substances for children under 3 years and pregnant women/ unborn children.
- Hazard assessment of the identified substances and determination of tolerable exposure levels (derived no effect levels, DNELs) for each substance.
- Assessment of risk in relation to the estimated exposure and an assessment of risk by simultaneous exposure to several substances with the same mode of action.
- Discussion of the risk assessments and identification of substances with highest impact in relation to risk for endocrine disruption and chronic neurotoxic effects.

The project also includes an analytical program to fill out knowledge gaps identified in the exposure assessment in order to obtain a better basis for the risk assessment of these substances. Furthermore, a condensed regulatory status and overview is given for the identified substances of concern.

As the intention of the project is to include as many substances as possible to illustrate the overall exposure, the starting point is as far as possible to use existing assessments or reviews of the identified substances, e.g. assessments by the European scientific expert groups/ committees regarding assessment of chemical substances in foods, cosmetics and consumer products. Next, the aim is to apply the knowledge that during many years of efforts has been accumulated in the Environmental Protection Agency from the many surveys and investigation projects, including the LOUS projects. Not least, the following projects have been relevant for the preparation of this project: ”Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products” (Danish EPA 2009); ”Exposure of pregnant consumers to suspected endocrine disruptors” (Danish EPA 2012a) and ”Survey and risk assessment of toluene and other neurotoxic substances in children´s rooms” (Danish EPA 2016a).

Identification of substances with endocrine disrupting and neurotoxic effects

The identification of endocrine disruptors, suspected endocrine disruptors and known neurotoxic substances in this project is based on information collected by the Environmental Protection Agency as well as knowledge from the scientific literature. The identification/ selection phase includes an initial qualitative assessment of whether the exposure to a substance of concern for the identified target groups was considered realistic. In the selection of the substances, emphasis is primarily on the inclusion of substances for which there is sufficient evidence of the substance's harmful effects on the endocrine system and/ or the nervous system, so that the toxicological background data on the substances can form the basis for a subsequent hazard assessment and risk assessment. The Danish proposal for criteria for identifica-

tion of hormone disrupting substances from 2011 is used in this project to determine if a substance is an endocrine disruptor or a suspected endocrine disruptor (Danish EPA 2011a). In the following, the wording “hormone disrupting substance” is used as an overall term for the groups of substances that are either “suspected hormone disrupting substances” or “hormone disrupting substances” according to these criteria. This process means that only a subset of neurotoxic, suspected endocrine disruptors and endocrine disruptors have been evaluated in the project. Thus, a number of endocrine disruptors and suspected endocrine disruptors have been identified but deselected for the risk assessment for a number of reasons, as described in Appendix 2. For example, for several groups of substances, indications of endocrine disrupting potential have been found, but sufficient data have not been found to determine the DNEL. This applies to several brominated flame-retardants, perfluorinated substances and some phenols. A number of pesticides with suspected endocrine disrupting potential are omitted because of low exposure, while some individual substances having suspected endocrine disrupting potential have been omitted because the mode of action was not considered suitable for grouping with antiandrogenic, estrogenic or thyroid hormone disrupting substances.

The terms "suspected endocrine disrupting" and "endocrine disrupting" substances reflect how strong the evidence is for endocrine disrupting effects of a substance. The Danish proposal for criteria for the identification of endocrine disrupting potential from 2011 is used in this project (Danish EPA 2011a). In this report, the term "endocrine disruptors" is used for the total group of substances that is either "suspected endocrine disrupting" or "endocrine disrupting" according to these criteria.
Similarly, some well-known neurotoxic substances have also been deselected. This has been done either because they are considered not relevant to this project (methanol, ethanol, and manganese), or because it is not considered possible to conduct a risk assessment of the substances, as there is no precise knowledge on the dose-response relationship and NOAEL/ LOAEL regarding their neurotoxic effects for the substances (e.g. arsenic, fluoride and particulates (air pollution)). The justification for these deselections is specified in Appendix 3.
Overall, 37 substances were included regarding endocrine disrupting effects and 39 substances regarding chronic neurotoxic effects, with some overlap (7 substances) between the groups.

Exposure data
The available exposure data collected are as far as possible divided into the different sources of exposure:

- food items including drinking water
- indoor environment (dust, vapours) + outdoor environment (soil)
- cosmetics
- consumer products (articles, toys, chemical products, etc.)
-

In relation to *food exposure* it is characteristic that the entire population is exposed to a greater or lesser extent, and therefore, a risk assessment based on food exposure cover a large fraction of the entire population and any specific subgroups (this may be data on different age groups or groups with different food preferences).
Such representative data as for food exposure is only rarely available for the *indoor environment and the outdoor environment*. The report's estimates for indoor environment/ outdoor environment must therefore be considered with greater caution as the contribution from the indoor environment can be very variable and depends on many factors, such as the age of the building, building materials used, furniture, and activities of the residents. For the outdoor environment, polluted soil will typically be important for the exposure of children under 3 years.

For *cosmetics*, just as for foods, any consumption/use of the product also leads to exposure to the ingredients contained in the product. Knowledge of substance content in a cosmetic prod-

uct and knowledge concerning use will give a fairly accurate indication of the exposure of the individual consumer. The degree of public exposure will to a greater extent than food exposure be determined by preference, as the use of cosmetics varies much in the population, i.e. some may not use other cosmetics than toothpaste and soap/ shampoo, while others have a high consumption of various cosmetic products.

Exposure from *consumer products* is as for cosmetics highly dependent on consumer preferences in relation to the purchased products, as well as the way they are used. The exposure estimates for consumer products are thus largely based on various assumptions, as the methodology for exposure estimation for consumer products are substantially less standardised than for foods and cosmetics. The exposure estimation often includes series of assumptions, each of which is subject to various degree of uncertainty.

Thus, from the collected data, the exposure for the individual substances is specified for each of the above sources, and the total exposure is calculated for the target groups, i.e. for children under 3 years and for pregnant women/ unborn children. Both medium exposure (characterised by the typical consumer exposure, e.g. an average or median exposure) and high exposure (i.e. an upper but realistic exposure such as a 95-percentile level) are calculated for the substances as far as possible. In addition, for some substances data could be obtained for specific exposure scenarios, typically worst-case scenarios, which are assessed separately from the other exposure.

In comparison with exposure estimations based on calculation models, biomonitoring studies containing exposure estimates were collected as well. Here the focus was on biomonitoring studies conducted in Denmark or from neighboring/ comparable countries and on studies in which the data has been converted to external daily exposure.

When reviewing these studies, estimation of exposure levels based on urine measurements were found for acrylamide, bisphenol A, phthalates (DEHP, DBP, DIBP, BBzP, DINP), triclosan and the UV filter BP-3, respectively. Especially for phthalates, there are highly relevant biomonitoring studies in both children and adults, where exposure estimates based on the measured data are indicated. These, together with the modelled exposure calculations, will help to provide a more complete picture of the exposure of the population groups.
For biomonitoring studies with urine data, it was observed that the detected measurements in general result in comparable or lower exposure estimates than the exposure estimates based on the modelled calculations for assessment of exposure from the different sources.

For biomonitoring studies in media other than urine, e.g. in breast milk these data resulted in high exposure levels for breastfed infants. Exposure estimations in these studies are based on the measured concentration of breast milk coupled with the intake amount of breast milk for infants, and this indicates that breastfeeding can be a significant source of exposure. Also, this type of exposure may be compared to exposure for non-breastfed infants where the exposure estimation relies on the modelled data based on content in food items and other sources. Thus, biomonitoring based exposure estimations for perfluorinated substances, for tetra-BDE-47, penta-BDE-99 and for totalPCB (sum of 7 PCB congeners) resulted in higher exposure via breast milk compared to alternative scenario regarding modelled exposure via food items. As the studies are not based on data from Danish mothers, they may not be directly transferable to the Danish population, but still they indicate that infants who are breastfed may be subjected to high exposure to substances that have accumulated in the mother. However, there are important benefits from breast feeding infants and these are generally considered to outweigh a potential risk from the chemical exposure.

Hazard assessment, determination of DNEL

It is necessary to have knowledge of dose-effect relationships for the neurotoxicity and/ or endocrine disrupting effects of the substances, in order to calculate a tolerable human exposure level (DNEL value) based on a NOAEL or LOAEL (or a benchmark dose) using assessment factors in accordance with the guidelines for their use. As for exposure estimation, uncertainties and limitations have to be considered as well when determining DNEL values.

For endocrine disruptors, all DNELs are determined based on animal studies. The basis for the calculation of DNEL is dependent on experimental design, choice of doses and investigated endpoints. Thereby the determined DNEL values could be changed with increased knowledge base.

For neurotoxic substances, the starting points for DNEL calculation are very different. In one case, DNEL is determined based on a single limited study on newborn mice, where the behaviour of the animals is evaluated. In another case, DNEL calculation may be based on IQ testing of thousands of children and relationships between e.g. levels of lead in the blood and the IQ level of the children. Although a numerical DNEL value for both types of data may be obtained, a DNEL obtained from a large population of people exposed at different levels of course is of greater relevance and strengthen the validity of the risk assessment.

In addition, it is worth noting that the tolerable exposure levels are typically lower the more knowledge that have been obtained for a substance and its effects. For instance, the tolerable exposure levels over the years have been reduced in connection with the increasing knowledge for substances such as lead, mercury, dioxins/ PCB, acrylamide and bisphenol A.

For endocrine disruptors, it is currently discussed whether a lower limit on the effects of endocrine disruptors can be determined with reasonable certainty (whether there is a threshold value for the effects) and thus, whether robust tolerable exposure levels (DNELs) can be deduced. As an alternative method to assess the risk of exposure to endocrine disrupting substances has not yet been developed, a traditional risk assessment approach is used here as described below. An advantage of this approach is that the risk of the combined exposure to multiple substances with the same modes of action can be calculated. If in future an agreement can be reached on alternative ways to assess the risk of endocrine disruptors, the calculations in this report should be reviewed. Such alternative risk assessment methods will be expected to result in lower DNEL values and thus higher calculated risk.

Risk assessment

In order to assess risk for a substance, there must be data to conduct both exposure assessments and hazard assessments. Risk assessments for 34 substances regarding endocrine disrupting effects and 29 substances regarding chronic neurotoxic effects could be carried out, corresponding to 56 substances, as there was an overlap of 7 substances between the groups. For the risk assessment, the risk characterisation ratio, RCR, is calculated based on the ratio between the overall exposure to the substance from all sources and the tolerable exposure level (DNEL):

RCR = exposure (µg/kg/d) / DNEL (µg/kg/d)

In this project, also the overall RCR value for all substances with the same types of effect is added to obtain an expression of the overall risk of simultaneous exposure for multiple endocrine disrupting/ neurotoxic substances. Simultaneous exposure to multiple chemical substances will typically be the case in food content and content in drinking water and soil/ dust where multiple agents may occur simultaneously, just as a person can also be exposed to substances from various consumer products simultaneously.
The overall risk can be expressed by adding the RCR values for the substances having the same mode of action:

$$RCR(total) = RCR(substance1) + RCR(substance2) + RCR(substance3) \ldots$$

Such RCR (total) values must be assessed with great caution, as the uncertainties for the individual RCR values are also added.
Addition of RCR values for multiple substances is performed for medium exposure (i.e. typical exposure) as well as for high exposure to the substances. However, method is considered most credible when adding medium exposure RCRs, as it seems less likely to be subjected to upper level exposure for many substances simultaneously.

Assessment of endocrine disrupting effects
The following table lists the RCR values for the substances with the highest RCR values for endocrine disrupting effects, as well as the total RCR value of the entire group.

Table of endocrine disruptors' contribution to RCR (medium and high exposure) and sources of the exposure to children under 3 years and pregnant women/ unborn children (RCR values above 0.1 are in italics and RCR values above 1 are marked in bold.

Substance	***Sources***	**RCR (medium exposure)**	**RCR (high exposure)**
		Children under 3 years/unborn children	**Children under 3 years/unborn children**
	Antiandrogenic substances		
PCBs and dioxins	Foods	***1.06****/0.53*	***2.3/1.15***
PCB total	Dust	-/-	*0.45/-*
DEHP	Foods, indoor environment, products	*0.35/0.12*	***1.61****/0.37*
DBP	Foods, indoor environment, products	*0.33/0.13*	***1.79****/0.44*
DiBP	Foods, indoor environment, products	*0.28*/0.098	***2.26****/0.33*
Paracetamol	Medicine	***25/33.3***	***100/133.3***
PFOS	Foods, indoor environment	*0.018/0.006*	*0.047/0.015*
Sum: RCRtotal_aa (with paracetamol)		***27/34.2***	***108/135.7***
Sum: RCRtotal_aa (without paracetamol)		***2.1****/0.9*	***8.5/2.3***
DEHP, biomonitoring		*0.14*/0.045	*0.56/0.15*
DBP, biomonitoring		*0.53*/0.081	***1.9****/0.2*
DiBP, biomonitoring		*0.38/0.2*	***1.9****/0.37*
PFOS, breast milk		*0.25/-*	*0.68/-*
	Estrogenic substances		
Butyl- and propyl paraben	Cosmetic products	*0.95/0.19*	***2.95****/0.8*
Bisphenol A	Foods, consumer products	0.097/0.054	*0.28/0.27*
Bisphenol A* (alternative DNEL)	Foods, consumer products	*0.55/0.31*	***1.58/1.52***

Substance	*Sources*	RCR (medium exposure) Children under 3 years/unborn children	RCR (high exposure) Children under 3 years/unborn children
Nonylphenol	Foods, indoor environment	0.053/*0.34*	*0.13/0.68*
BP-3	Cosmetic products	*0.18*/0.077	*0.35/0.15*
OMC	Cosmetic products (incl. sunscreen)	*0.84/0.36*	***1.68***/*0.72*
Siloxane D4	Cosmetic products	-/0.052	*-/0.11*
Sum: RCRtotal_estr		***2.1/1.1***	***5.4/2.8***
Butyl- and propyl paraben, biomonitoring		0.015/-	0.019/-
Bisphenol A, biomonitoring		0.017/0.01	0.071/0.06
Bisphenol A* (alternative DNEL), biomonitoring		0.094/0.06	*0.40/0.34*
BP-3, biomonitoring		<0.001	<0.001
	Thyroid hormone disrupting substance		
BHA	Foods	*0.23/0.13*	*0.57*/***1.14***
BHT	Foods, cosmetics	*0.44/0.17*	***1.5/1.04***
PCBs and dioxins	Foods	*0.35/0.18*	*0.77/0.38*
DEHP	Foods, indoor environment, products	0.047/0.015	*0.21*/0.049
OMC	Cosmetic products (sunscreen)	***1.4***/*0.6*	***2.8/1.2***
Triclosan	Indoor environment	*0.25/0.24*	***1.0***/*0.73*
PFOS	Foods, indoor environment	0.014/0.005	0.038/0.012
Sum: RCRtotal_thyr		***2.8/1.3***	***7.0/4.6***
DEHP, biomonitoring		0.018/0.006	0.075/0.019
PFOS, breast milk		*0.20*/-	*0.54*/-

- indicates that no relevant data were found.

** For bisphenol A, RCR values are also indicated calculated by using alternative, lower DNEL (DTU 2015, see Appendix 7a).*

When adding RCR values for medium exposure to endocrine disruptors, overall *RCRtota*l values were calculated for both antiandrogenic, estrogenic and thyroid hormone disrupting substances resulting in values just above 2 for exposure of children under 3 years with respect to all three types of effects. These values indicate that the overall exposure of children under 3 years to endocrine disruptors may be of concern even at average exposures.
For pregnant women/ unborn children, the *RCRtotal* values at medium exposure were just below 1 for antiandrogenic substances, and just above 1 for estrogenic and thyroid hormone disrupting substances, respectively. These values indicate that the overall exposure of pregnant women/ unborn children to endocrine disruptors may be of concern even at average exposures, especially when it is considered that several other endocrine disruptors are not included in the estimations. Furthermore, these results – due to indication of concern - emphasize that it may be important to improve/ refine the risk assessment by obtaining more knowledge about exposure and toxicity of the substances.

For the endocrine disrupting effects, the project found that the intake of paracetamol at critical periods during the early development may result in a potential risk of antiandrogenic effects.

RCR values for Paracetamol exceed the RCR values for the other substances, but it should be noted that the risk assessment has been performed using the same principles as for environmental or food-related substances to relate risk calculation for endocrine disrupting activity of other chemicals to other sources of possible endocrine disruption. Risk assessment of medical products will generally be different from risk assessment of chemicals from food, cosmetics, indoor climate and consumer products, as medicine may have acceptable side effects, and as risk assessment is to a larger extent based on available human studies.
Here, risk assessement of environmental or food-related substances is based on animal studies and uncertainty factors are applied in the calculation of the doses that can be considered tolerable for humans. This is not common practice in the pharmaceutical field, which more often is based on studies in humans. The Danish Medicines Agency evaluates that paracetamol is far better studied in humans than environmental substances are, and that the dose is more controlled.
The Danish Medicines Agency points out that the European Medicines Agency, the Pharmacovigilance Working Party and Pharmacovigilance Risk Assessment Committee (PRAC) have concluded that based on available studies and data there is currently not sufficient evidence for a link between paracetamol and anti-androgenic effects.
The Danish Medicines Agency points out that when during pregnancy there is a need for pain medication, it is still recommended to use paracetamol as this type of painkiller is estimated to be less harmful to the unborn child than other types of painkillers such as ibuprofen. It is recommended only to take paracetamol at medical need, at the lowest possible dose and for the shortest possible time, as is the recommendation for all medicincal products administered during pregnancy.

PCBs and dioxins contribute with high RCR values. For children below 3 years, the intake of PCBs and dioxins in foods may exceed the tolerable exposure levels and thus cause concern.

The relatively high RCR values by exposure to certain phthalates (*DEHP, DBP, DIBP*) in food, indoor environment and consumer products contribute significantly to the overall concern of endocrine disrupting effects. There is good agreement between the modelled exposure data and the estimates based on biomonitoring data. Thus, it is considered likely that a proportion of children and pregnant women/ unborn children is subjected to exposure levels of concern at an overall risk assessment of antiandrogenic substances.

Bisphenol A from food and consumer products contributes significantly to the total RCR values, and particularly by use of the *alternative, low DNEL* (DTU 2015), bisphenol A exposure alone can be of concern.

BHA and BHT in food are seen to contribute significantly to the overall RCR, and in the scenario with high intake, these substances alone can be of concern regarding endocrine disrupting effects. In this project, the content of BHT was measured in a variety of creams (whereas BHA only in one single body oil) indicating that there may be a significant contribution from BHT in cosmetic, although there is considerable uncertainty associated with the systemic exposure calculations for BHT in cosmetics, because of limited knowledge on absorption and metabolism in the body by dermal exposure.

For *butyl- and propyl paraben and OMC,* high RCR values are seen indicating possible concern, especially for children under 3 years. It should be noted that butyl and propyl paraben are included in the exposurescenarios for children although these parabens are no longer allowed in cosmetic products intended for children below 3 years (national ban). Furthermore, these figures are mainly based on exposure scenarios with high content in cosmetic products (not intended for children specifically), and it must be assumed that only a small part of the Danish children/ unborn children are exposed to such high exposures of concern. It is not clear whether these substances are typically used in the maximum allowable concentrations, and it

should be noted that a lower actual content would result in lower RCR values. This conclusion is supported by the fact that the RCR values based on biomonitoring data are lower than the RCR values based on the modelled exposures. Although there are a number of uncertainties by using biomonitoring data to estimate exposure (e.g. how the substances are distributed in the body, which metabolites are formed and whether they are measured, and how they are excreted), this could indicate that the actual exposure is lower than the theoretical estimates. For triclosan, dust in the indoor environment was identified as a potential source to exposure of children with an RCR values about 1, while pregnant women/ unborn children in may be exposed through the few brands of toothpaste containing triclosan.
Furthermore, it is seen that PFOS in breast milk may contribute to the overall risk for hormone disrupting effects, while exposure through food, dust and air only make slight contributions to the overall RCR values. However, there are important benefits from breast feeding infants and these are generally considered to outweigh a potential risk from the chemical exposure.

Assessment of chronic neurotoxic substances
The project has identified the most important neurotoxic substances in the table below, i.e. the substances with the strongest documentation for chronic neurotoxic effects combined with the highest calculated RCR values. The table also indicates the main sources of exposure and the calculated RCR values for children under 3 years and pregnant women/ unborn children at medium and high exposure, respectively.

Table of neurotoxic substances that contribute mostly to RCR (medium exposure, high exposure) and sources for exposure of children under 3 years and pregnant women/ unborn children.

Neurotoxic substance	Sources	RCR Medium exposure children/ pregnent women	RCR High exposure children/ pregnent women
Lead	Foods, dust/ soil, articles	51.2 / 4.8	231 / 16.8
Bisphenol A	Foods, articles	2.4 / 1.4	5.49 / 6.66
Dioxins and dioxin-like PCB	Foods	1.05/ 0.53	2.30 / 1.15
Acrylamide	Foods	0.41 / 0.15	0.71 / 0.29
Mercury	Foods	0.27 / 0.03	0.44 / 0.11
Methyl mercury	Foods	0.21 / 0.10	1.21 / 0.27
RCR total (for the substances above)		***56 / 7.2***	***242 / 25.8***
PCBtotal	Breast milk, breast feeding	40 / -	109 / -
Dioxins and dioxin-like PCB	Breast milk, breast feeding	131 / -	- / -
PFOS	Breast milk, breast feeding	0.67 / -	1.8 / -

When adding the RCR values for medium exposure to all neurotoxic substances (also substances of minor importance not included in the table), overall RCR values of 61.1 for exposure of children under 3 years and of 7.9 for exposure of pregnant women/ unborn children were calculated. These high values indicate that especially children under 3 years, but also unborn children, are exposed to neurotoxic substances in doses of concern regarding risk of neurotoxic effects.

For the *neurotoxic substances*, it is seen that exposure to *lead* by far causes the greatest risk for neurotoxic effects among all studied neurotoxic substances. Exposure to lead can be divided in the sources: food + drinking water (particularly drinks, but also fruit, vegetables and cereals represent the largest contribution to the exposure), soil/ dust and, migration of lead from lead containing articles and items that children come into contact with or put in the mouth (mouthing). Strict regulatory measures, however, may reduce lead exposure further in the coming years.

For the documentation of neurotoxic effects lead, several well-conducted epidemiological studies - mainly from the US – have demonstrated the correlation between lead exposure to the unborn child and infants and reduced IQ measured at higher age. Based on this very high RCR value for lead, it seems important continuously to follow the development in content of lead in food items and articles. Measuring of lead levels in the blood of children and pregnant women would also give a more accurate picture of the actual exposure to lead and thus, the risk for neurotoxic effects.

Also, exposure to dioxins and PCBs through foods gives cause for concern regarding chronic neurotoxic effects, where especially children under 3 years who are breastfed can achieve significantly elevated RCR values as a result of exposure through breast milk. However, there are significant advantages for the child being breastfed that are generally considered to outweigh/ overshadow the potential risk from exposure to PCBs and dioxins in breast milk. To obtain a more precise knowledge and balance of this aspect for Danish conditions, it would require measurements of PCBs and dioxins in breast milk of Danish women, as such data are not present. With respect to PCB exposure from indoor environment due to use of PCB-containing building materials the data are considered too limited to assess the risk for neurotoxic effects. This exposure will be dominated by the lower and most volatile PCB congeners, for which sufficient data on neurotoxicity and DNEL determination could not be found.

For *mercury and methyl mercury,* exposure through food (methyl mercury mainly from fish) causes a contribution that should be considered when looking at the overall impact from neurotoxic substances. For children under 3 years, exposure may exceed the tolerable level of exposure. A specific contribution to mercury exposure may occur from broken energy saving light bulbs. However, such exposure can be avoided by careful removal of the broken bulb and by ensuring a thorough ventilation of the room.

Finally, increased risk of neurotoxic effects was calculated due to exposure to *bisphenol A*. Here, the primary exposure is through food items, but there may also be exposure from the indoor environment and articles. Especially exposure through cash receipts may for specific high exposure scenarios exceed the tolerable exposure level in pregnant women. However, the use in cash receipts is no longer allowed from January 2020. For children under 3 years, a potential content in pacifiers may be a cause for increased risk. The assessment of bisphenol A is associated with uncertainty, especially because the EU expert committees (EFSA and RAC Committee in ECHA) disagree on whether data regarding neurotoxic effects are sufficient for use in the context of a quantitative risk assessment. The risk assessment in this report uses the RAC Committee's DNEL value for the neurotoxic effects of bisphenol A.

In addition, the project identified a number of several other neurotoxic substances (e.g. certain brominated and chlorinated flame-retardants, PFOA and PFOS, aluminium, and organic solvents and certain pesticides). The exposure to many of these substances is difficult to assess, but each could make a contribution to the overall risk, although to a lesser extent than the previous mentioned neurotoxic substances.

Finally, it should be mentioned that the assessment of effects from a number of other potentially neurotoxic substances, such as alcohol, particle exposure from smoking or from ambient air pollution, or exposure to inorganic fluoride or arsenic are not included in this project.

Chemical analysis of selected products and risk assessment

In the project, it was decided to choose cosmetic products for analysis of BHA and BHT and pizza boxes for analysis of bisphenol A, S, F, and of phthalates, in order to make risk assessment of these products from the measured data

Cosmetics containing BHA and BHT

The measurements indicated that only one product (a body oil) contained BHA, whereas several products contained BHT in concentrations up to 0.32 % (in sunscreen) and 0.23 % (in body lotion). It should be noted that there is insufficient knowledge about the absorption of BHT through the skin, but in order to calculate the RCR values, a maximum dermal absorption rate of 4 % is used (data from a study with dermal exposure of guinea pigs). From this it was shown that BHT in cosmetic products does not pose a risk when one product is used, but potentially contributes to the overall RCRthyr, as values by using body lotion and sunscreen will cause RCRthyr values for BHT of 0.3 and 0.2 for children under 3 years and pregnant women/ unborn children, respectively**.**

Pizza boxes containing bisphenol A and phthalates

In pizza boxes, contents of bisphenol A and the phthalates DEHP, DINP, BBP, DiBP, DBP and DNOP was found in analyses where pizza cardboard were "dissolved" in 50 % ethanol. In the migration test with heating of the pizza box (corresponding to a hot pizza) and collection of released substance from the cardboard in Tenax powder spread on the cardboard, no content of any of the substances could be found in the Tenax powder (above the method's detection limit).

Thus, it was not possible to make a more precise risk assessment regarding exposure in connection with release of the substances from the pizza boxes.

Overall conclusion

Despite uncertainties regarding the selection of substances having endocrine disrupting or neurotoxic effects the project result is considered to give a fairly good indication of the most critical substances in terms of increased risk for endocrine disrupting and neurotoxic effects in relation to children under 3 years and pregnant women/ unborn children. Furthermore, it was found that for a number of substances, it was not possible to assess the risk, due to lack of knowledge either regarding human exposure or regarding dose-response relationship for the adverse health effects.

Among the evaluated substances, the most significant endocrine disruptors that children under 3 years and pregnant women/ unborn may be exposed to are: *dioxins/ PCBs, phthalates (DEHP, DBP, DiBP), bisphenol A, BHA, BHT*, where the risk level for each substance is relatively comparable, and where exposure mainly comes from food items and thus is likely to be recurring. For propyl and butyl paraben and OMC there may be cause for concern regarding exposure from cosmetics, as exposure to larger quantities of products with high contents of these substances in a sensitive period of the development may result in risk of endocrine disrupting effects.

The medicinal product paracetamol contributes with far the highest RCR value for endocrine disruption. In this report, risk assessment for paracetamol was performed using the same principles as for environmental or food-related substances, where uncertainty factors of 100 are applied, and based on high doses. At present it is not clear when during development, or for how long time such exposure should last in order to contribute to a possible risk for adverse effects later in life. The Danish Medicines Agency points out that the European Medicines Agency (EMA) has repeatedly assessed the available data and studies in humans and animals, and did not find sufficient evidence for a relationship between paracetamol and antiandrogenic effects. Therefore, the Danish Medicines Agency still recommends paracetamol as first-line treatment of pain for pregnant women and children.

Among the evaluated substances, the most significant chronic neurotoxic substances that children under 3 years and pregnant women/ unborn children may be exposed to are lead, dioxins/ PCBs, mercury/ methyl mercury, bisphenol A and acrylamide. Lead constitutes by far the highest risk of the chronic neurotoxic effects. For all of these substances, exposure through food is the most significant source. For lead significant exposure also occurs through drinking water, soil and lead containing metal objects that may be subject to mouthing by children. Although these estimates may be somewhat overestimated for the specific sources due to conservative assumptions this this is not considered to significantly change the overall picture as lead as the substance of most concern.
Breast milk must also be considered a major source of dioxin/ PCB exposure.

The above conclusion is based on a screening of substances, that are considered relevant in relation to exposure of children under 3 years or pregnant women/ unborn children, and at the same time is considered to have endocrine disrupting and chronic neurotoxic effects. For over 60 of such substances, data have been collected regarding exposure, hazards and tolerable exposure levels for the substances.

The result of the risk assessments is estimated to have resulted in the identification of the most critical substances. For some areas with identified risk, there may be a need for further detailed analysis of this risk. This applies to children and pregnant women's exposure to lead, where the high identified risk could be examined ands substantiated further through biomonitoring data from children and prenant women. Similarly, breast milk analyses on PCB and dioxin could give a better picture of the significance of infants' exposure through breast milk.
It has generally been difficult to obtain an accurate assessment of exposure through indoor environment and consumer products/ articles, as representative knowledge on general population exposure through these sources is very incomplete.

Finally, the exposure assessment for pregnant women or women of childbearing age in this project has only focused on the exposure as a consumer in connection with food, cosmetics and consumer products. Women of childbearing age or pregnant women may also be exposed to endocrine disrupting/ neurotoxic substances through other sources, e.g. in connection with exposure in the working environment, trough alcohol consumption or smoking, or in connection with medicinal products.

1. Introduction

1.1 Background and objective

The Government and the political party “Enhedslisten” want to safeguard children and young people against harmful and unnecessary chemistry. As part of this effort, the Environmental Protection Agency in 2013-2015 undertook a number of different initiatives, such as information campaigns regarding regulation on toys, cosmetics, electronics and textiles directed towards for companies, and on control of chemicals in products for children as well as identification and risk assessment of chemicals in products for children.

It is therefore natural in connection with the finalization of the many initiatives in 2017 to gather the data obtained from these efforts and make an updated assessment on the children's overall exposure and risk from chemicals of high concern.

The objectives of the project are therefore:

- Based on the results of surveys and controls undertaken under the Danish EPA’s child chemistry package to estimate the overall exposure of children, pregnant women/ unborn children to chemical substances that are endocrine disruptors, suspected endocrine disruptors or neurotoxic.

- To identify chemicals that are endocrine disruptors or suspected endocrine disruptors based on a gross list from the Danish EPA. The substances should be identified based on a number of criteria, including the possibility of setting a NOAEL/ LOAEL/ BMDL for endocrine disrupting effects, and whether there is an anticipated exposure of children and pregnant women/ unborn children to the substances. In the report the wording “hormone disrupting chemicals” is used as an overall term for hormone disrupting chemicals as well as suspected hormone disrupting chemicals.

- To identify neurotoxic chemicals for which exposure of children and pregnant women/ unborn children is likely.

- To examine whether there is available literature on children’s and unborn children’s exposure to the selected substances.

- To perform relevant chemical analyses of selected products to obtain data for more accurate assessments of the exposure potential.

- To exame whether individual sources/ exposure may pose a risk and/ or whether the total exposure from several sources/ chemicals may pose a risk.

The focus is on children under 3 years and pregnant women/ unborn children. Thus, the project should provide knowledge of children up to 3 years and pregnant women/ unborn children's overall exposure to chemical substances that are endocrine disruptors, suspected endocrine disruptors or neurotoxic, and make assessment of the possible associated risks.

1.2 Implementation of the project

For overall understanding of the project's activities, the implementation and contents, the project can be described based on the following content of the chapters:

In Chapter 2 "*Preliminary selection of substances with endocrine disrupting, suspected endocrine disrupting or neurotoxic effects*", the first selection/ screening is made for substances that are considered endocrine disruptors, suspected endocrine disruptors or chronic neurotoxic. The selection is partly based on whether there is sufficient evidence of the substance's harmful effects (endocrine disrupting effects or chronic neurotoxic effects) coupled with an initial knowledge regarding relevant sources of exposure of children and pregnant women/ unborn children for the substances.

In Chapter 3 "*Selection of data for exposure assessment*", additional data are searched and gathered regarding exposure to the substances, for further assessing the extent of the exposure and to make specific exposure assessments for children and pregnant women/ unborn children.

Chapter 4 "*Regulation of the selected substances*" describes the way in which the selected substances are regulated and determines any requirements that apply to the use of the substances, particularly in the area of consumer products (food, cosmetics, toys etc.)

In Chapter 5 "*Analysis of selected substances in selected products*", specific products are selected based on identification of data gaps from knowledge in the preceding chapters. Further analysis of the content/ release is made on specific substances, to obtain more precise knowledge of exposure and risk assessment of the products in connection with children and pregnant women/ unborn children.

In Chapter 6 "*Exposure assessments*", an overview is made of the exposure sources and exposure levels relevant for children and unborn children/ pregnant women regarding the substances for which exposure data have been collected in Chapter 3, as well as from the data obtained from the analyses in Chapter 5.

In Chapter 7 "*Hazard Assessment of selected substances*", the critical effects and dose levels are identified for the identified endocrine disruptors, suspected endocrine disruptors and the neurotoxic substances. Tolerable exposure levels (TDI/ DNEL values) are set - if possible - for the substances, and furthermore it is assessed whether the substances can be grouped based on modes of action, and how this aspect can be considered in the risk assessment.

In Chapter 8 "*Risk Assessment*", the levels of exposure for children and unborn children/ pregnant women (Chapter 6) are compared with the tolerable levels of exposure to the (Chapter 7), and it is assessed whether the exposure poses a risk for endocrine disruption, suspected endocrine disruption or chronic neurottoxic effects. It is assessed which specific sources of exposure to each substance constitute a risk, or whether the overall cumulated exposure to substances with the same mode of action poses a risk.

Chapter 9 "*Discussion and Conclusion*", summarises and discusses the main findings of the risk assessment, taking into account the most significant uncertainties and limitations assessed to be related to the specific assessments.

It is concluded which substances are considered especially to contribute to the risk of endocrine disrupting and neurotoxic effects to children and unborn children.

Appendices

As background for the individual chapters, data have been collected, listed and assessed in Appendices 1-9 to this report. The extensive tabular material included in the appendices should be seen as a working tool in terms of systematisation and assessment of data, and also describes the stepwise workflow during the preparation of this report. The appendices refer back to the original references as not all necessarily appear in the reference list to the main report that predominantly make reference to the overview literature or expert reports in which the original literature has been assessed. As the appendices are largely considered to be working documents, and as several people have been involved in the preparation of the appendices, the filled out tables for the many substances may not be completely identical in terms of detail and description. Within this project's resources, focus has been on the listing and the further use of data in the project rather than obtaining 100 % consistency in the presentation in the appendices.

2. Preliminary selection of substances with endocrine disrupting, suspected endocrine disrupting or neurotoxic effects

2.1 Overall strategy for selection of substances for risk assessment in the project

This project focuses on children under 3 years and pregnant women/ unborn children's exposure to chemicals with endocrine disrupting or neurotoxic effects. In the report the wording “hormone disrupting chemicals (or effects)” is used as an overall term for hormone disrupting chemicals (effects) as well as suspected hormone disrupting chemicals (effects). Exposure of children and pregnant women/ unborn children to substances that may affect the natural endocrine balance, or can damage the nervous system, is considered particularly critical, as the hormone-regulated developmental processes of organs and the development of the central nervous system in children and unborn children are particularly vulnerable processes.

In this chapter, a gross list of relevant substances will be selected and this will form the basis for further selection and subsequent assessment of children’s and unborn children's overall exposure to the substances.

In the selection of the substances, emphasis is primarily on the inclusion of substances for which there is sufficient evidence of the substance's harmful effects on the endocrine system and/ or the nervous system, so that the toxicological background data for the substances can form the basis of a subsequent hazard assessment and risk assessment. The proposed Danish criteria from 2011 for identification of a substance as an endocrine disruptor or suspected endocrine disruptor have been used (Danish EPA 2011a).

In the e selection of the substances, chemicals are prioritised based on our current knowledge for an exposure potential in relation to children under 3 years and pregnant women/ unborn children, i.e. knowledge concerning use in various consumer products such as food, food packaging material, cosmetics, toys and presence in indoor environment. Exposures through special nutritional supplements and prescription medicine are not covered, whereas self-medication with non-prescription medicine is covered.

In the selection of the substances, the objective is to make use of the compiled knowledge gathered through the Environmental Protection Agency's many projects in recent years in connection with the large number of number of survey projects (146 reports since 2001) and review projects, including the 40 LOUS projects carried out in the period 2012-2015.

However, specific attention should be paid to the knowledge from the following project reports:

- ”2 year old children's exposure to chemicals” (Danish EPA 2009)
- ”Pregnant consumer’s exposure to suspected endocrine disruptors” (Danish EPA 2012a)
- ”Survey and risk assessment of toluene and other neurotoxic substances children’s rooms” (Danish EPA 2016a)

2.2 Strategy for selection of endocrine disruptors and suspected endocrine disruptors

The selection of endocrine disruptors is based on a gross list, which the Danish EPA attached to the tender of this project (see Appendix 1). This list is generated from the various lists of endocrine disruptors and suspected endocrine disruptors, including the REACH candidate list, the EU priority lists of suspected endocrine disruptors, ChemSec's SIN list and the REACH list of substances under substance evaluation (Corap). In addition, substances have been identified based on the knowledge that had been collected from the reports "Pregnant consumers’ exposure to suspected endocrine disruptors" and "2-year old children's exposure to chemicals". For other substances, overview literature was used and also specific literature about the substances, exposure and possible endocrine disrupting effect in experimental studies.

It should be noted, that the wording as “suspected endocrine disrupting” or “hormone disrupting” reflects the evidence of the hormone disrupting effects of a substance. The Danish proposal for criteria for identification of hormone disrupting substances from 2011 is used in this project (Danish EPA 2011a). In the following, the wording “hormone disrupting substance” is used as an overall term for the groups of substances that are either “suspected hormone disrupting substances” or “hormone disrupting substances” according to these criteria.

The pesticides with a potential of endocrine disrupting effects are selected based on the publication by Jensen et al. (2015), where pesticides with the most significant exposure (in terms of highest risk characterisation ratios) of the Danish population have been identified.

2.3 Selection of endocrine disruptors and suspected endocrine disruptors

Table 2.1 lists the substances that by the strategy described in Section 2.2 were selected based on knowledge of endocrine disruptors and possible exposure of children and pregnant women/ unborn children.

Table 2.1 List of endocrine disruptors and suspected endocrine disruptors and expected sources of human exposure to the selected substances.
Endocrine disrupting mode of action is indicated by the following codes: AA = anti-androgenic mode of action, E = estrogenic mode of action, T = thyroid hormone disrupting mode of action.

Substance group	Substance	Mode of action	Consumer products	Food	Indoor environ ronment	References
Antioxidants	Butylated hydroxyanisole (BHA)	T	X	X		EFSA 2012a
Antioxidants	Butylated hydroxytoluene (BHT) = 2,6-Di-tert-butyl-p-cresol (DBPC)	T	X	X		EFSA 2012a
Brominated	TBBPA (Tetrabromobisphenol A)	T	X		X	Danish EPA 2012a

Substance group	Substance	Mode of action	Consumer products	Food	Indoor environment	References
Brominated	HBCDD	T			X dust, air	ECB 2008
Brominated	Deca-BDE	T			X dust	
Chlorinated	Dioxins and dioxin like PCBs	AA, T		X	X	Danish EPA 2012a
Fluorinated	Perfluorooctanoic acid (PFOA)	T	X	X	X	Danish EPA 2012a
Fluorinated	Perfluorooctane sulfonate PFOS	T, AA		X	X	Danish EPA 2012a
Fluorinated	PFHxS	T		X	X	Tox: only unpublished data
Medicine	Paracetamol	AA	X			
Parabens	Propylparaben	E	X			Danish EPA 2012a
Parabens	Butyl paraben	E	X			Danish EPA 2012a
Phthalates	DEHP (di-ethyl-hexyl-phthalate)	AA, T	X	X	X	Danish EPA 2012a
Phthalates	DINP (di-iso-nonyl-phthalate)	AA	X	X	X	Danish EPA 2012a
Phthalates	DBP (di-butylphtalate)	AA	X	X	X	Danish EPA 2012a
Phthalates	DIBP (di-iso-butyl-phtalate)	AA	X	X	X	Danish EPA 2012a
Phthalates	BBP (butyl-benzyl-phtalate)	AA	X	X	X	Danish EPA 2012a
Phthalates	Dipentylphtalate	AA	X	?	X	Danish EPA 2012a
Phthalates	Di-n-hexylphtalate	AA		?	X	Danish EPA 2012a
Phthalates	Di-n-octylphtalate (DnOP)	AA, T	X	?	X	Danish EPA 2012a
Phthalates	DCHP	AA		X		ECHA 2016
Phthalates	DPHP	T	X	?		
Phenols	Bisphenol A	E	X	X	X	Danish EPA 2012a
Phenols	Bisphenol S	E	(X)	X	X dust	Rochester 2015. svagere evidens end for BPF
Phenols	Bisphenol F	T E	(X)	X	X dust	Rochester 2015
Phenols	Nonylphenol	E	x			Danish EPA

Substance group	Substance	Mode of action	Consum-er prod-ucts	Food	Indoor environ ron-ment	References
						2012a
Pesticides	Pirimiphos-methyl Procymidon Dithiocarbamater (Man-cozeb, Maneb, Pro-pineb) Diazinon Linuron	AA/E AA T E AA				Not all have high exposure acc.to article by Jensen et al., 2015
UV-filters	OMC (octyl methoxy-cinnamate or 2-ethylhexyl-4-methoxycinnamate)	E, T	X			Danish EPA 2012a
UV-filters	Benzophenone 3 (BP-3)	E	X			Danish EPA 2012a
Other	Triclosan	T, E	X	?		Danish EPA 2012a
Other	Octamethylcyclotetra-siloxane D4	E	X			Danish EPA 2012a

Some of the substances were included in the projects "Pregnant consumers' exposure to suspected endocrine disruptors" and "2-year-old children's exposure to chemicals". Some of the substances from these reports are not included here, as they are not considered relevant to exposure, e.g. certain pesticides, not shown in the article by Jensen et al., 2015; resorcinol, which provided only a negligible contribution to the project about pregnant women's exposure; and isobutyl paraben which has since been banned in cosmetic products. Among the new substances in this project are two phthalates (DHCP and DPHP), two bisphenols (bisphenol F and S), a perfluorinated substance (PFHxS), two brominated flame-retardants (HBCDD and Deca-BDE), two preservatives (BHA and BHT), 2 pesticides (diazinon and linuron), and a medicinal product paracetamol.

2.3.1 Discussion of data

The substances in Table 2.1 are selected for subsequent exposure assessment and risk assessment. The substances are also selected as possible candidates for cumulative risk assessment based on knowledge of estrogenic, antiandrogenic or thyroid hormone disrupting mode of action. It is initially assessed that there are sufficient data to determine the DNEL and enough knowledge about possible exposure of children and pregnant women/ unborn children.

A number of substances from the Danish EPA list (Appendix 1) in this initial phase were excluded due to insufficient data for risk assessment of relevant endocrine disrupting effects. These excluded substances are listed in Appendix 2 with description of the reason for the exclusion. Typically, there is insufficient knowledge about exposure, insufficient knowledge about endocrine disrupting effects for determining DNEL, or a reproduction adverse effect is believed to take place via a different mode of action (not estrogenic, antiandrogenic or thyroid hormone disrupting).

2.4 Strategy for selection of neurotoxic substances

The basis for the selection of neurotoxic substances in this project is substances for which there is evidence that they have resulted in chronic damage to the nervous system either in animals or in humans, either adults, children or unborn children.

In the selecting, especially the results from the "Survey and risk assessment of toluene and other neurotoxic substances in children's rooms" (Danish EPA 2016) are used as well as the references used in the preparation of this report.

2.5 Selection of neurotoxic substances

In the project "Survey and risk assessment of toluene and other neurotoxic substances in the children's rooms" (Danish EPA 2016a), a selection of substances was made regarding volatile organic compounds (VOC) with evidence for the substances' chronic neurotoxic effects. Also the substances were considered to have potential for exposure of both small and larger children in connection with evaporation from the interior, furniture, rugs, electronics and from toys in a child's room.

The selection of the volatile substances with neurotoxic potential was made based on substances identified as neurotoxic substances on the LOUS list (including LOUS reports for toluene, styrene, n-hexane and white spirit) and from the review of a number of key references in the area:

- DGUV, 2007. Polyneuropathie oder Enzephalopathie durch organische Lösungsmittel oder deren Gemische. Deutsche Gesetzliche Unfallversicherung BK 1317, BK-Report 2/2007.
- EC, 2009. Information notices on occupational diseases: a guide to diagnosis. Det Europæiske Arbejdsmiljøagentur, Directorate-General for Employment, Social Affairs and Equal Opportunities, European Commission.
- Giordano, G. and Costa, L.G., 2012. Review article – Developmental neurotoxicity: some old and new issues. International Scholarly Research Network, ISRN Toxicology, Volume 2012, Article ID 814795.
- Grandjean, P. and Landrigan, P.J., 2006. Developmental neurotoxicity of industrial chemicals. The Lancet 368.9553 (2006): 2167-2178.
- Grandjean, P & Landrigan PJ, 2014. Neurobehavioural effects of developmental toxicity. Lancet Neurol, 13, 330-338.
- JRC/ EU-Commission, 2013. Harmonisation framework for health based evaluation of indoor emissions from construction products in the European Union using the EU-LCI concept. EUROPEAN COLLABORATIVE ACTION URBAN AIR, INDOOR ENVIRONMENT AND HUMAN EXPOSURE. Environment and Quality of Life Report No 29.

Based on these sources, the Danish EPA (2016a) project selected 16 chronic neurotoxic substances (marked * in Table 2.2). The general background and documentation basis for this selection are described in Chapter 2 and Appendix 1 of the Danish EPA project (Danish EPA 2016a).
Regarding possible exposure, hydrocarbons were assessed to pose the greatest potential for exposure (evaporation from a number of articles and consumer products, including paints, turpentine, gasoline), while exposure to the chlorinated solvents is estimated to be more limited in relation to more specific exposure situations (Danish EPA 2016a).

Table 2.2 List of selected chronic neurotoxic substances

Neurotoxic substance	Other references	TDI or N(L)OEL	Potential exposure:		
			Consumer products	Food / drinking water	Indoor environment
Brominated substances					
HBCDD TBBPA BDE-47 BDE-99 BDE-209	Danish EPA-LOUS 2014e Giordano & Costa 2012; EFSA 2011(a+b+c)	+ +	(+)	(+)	(+)
Chlorinated substances					
Monochloromethane*	-	+N	(+)	÷	÷
Dichloromethane*	-	+N	(+)	÷	÷
Trichloroethylene*	-	+N	(+)	÷	÷
Tetrachloroethylene*	-	+N	+	÷	(+)
PCB	Danish EPA 2014a EFSA 2005 EFSA 2012e	+ +	÷	+	(+)
TCDD	EFSA 2012e SCF 2001	+ +	÷	+	÷
Fluorinated substances					
PFOS/PFOA	Danish EPA-LOUS 2013b US EPA 2016a+b EFSA 2008 Danish EPA 2015a	+ + +	(+)	+	(+)
Hydrocarbons					
n-hexane*	Danish EPA-LOUS 2014a	+N	+	÷	+
n-heptane*	-	+N	+	÷	+
Toluene*	Danish EPA-LOUS 2014b	+N	+	÷	+
Xylenes*	-	+N	+	÷	+

Neurotoxic substance	Other references	TDI or N(L)OEL	Potential exposure:		
			Consumer products	Food / drinking water	Indoor environment
Ethylbenzene*	-	+N	+	÷	+
Styrene*	Danish EPA-LOUS 2014c	+N	+	÷	+
Methylstyrene*	-	+N	+	÷	+
Propylbenzenes*	-	+N	+	÷	+
Trimethylbenzenes*	-	+N	+	÷	+
Diisopropylbenzene*	-	+N	+	÷	+
Phenyloctane*	-	+N	+	÷	+
White spirit C7-C12 hydrocarbons*	Danish EPA-LOUS 2014d	+N	+	÷	+
Metals					
Aluminium and compounds	SCCS 2014	+	+	+	÷
Lead and compounds	Danish EPA-LOUS 2014f EFSA 2010 ECHA/RAC 2011a	+N +N +N	+	+	(+)
Mercury and compounds	Danish EPA-LOUS 2014g EFSA 2012d ECHA/RAC 2011b	+ +N +N	(+)	+	÷
Pesticides					
Org. phosphates: Diazinon Dimethoate Chlorfenvinphos Methamidophos Oxydementon-methyl *Carbamates:* Carbaryl Benomyl	Jensen et al. 2015** EFSA 2013	+ +	÷	+	÷

Neurotoxic substance	Other references	TDI or N(L)OEL	Potential exposure:		
			Consumer products	Food / drinking water	Indoor environment
Methomyl					
Phenols					
Bisphenol A	Danish EPA-LOUS 2013a EFSA 2015b ECHA/RAC 2015a	 + +	+	+	÷
Other substances					
Acrylamide	EFSA 2015a	+N	(+)	+	÷
Tricresylfosfate	Danish EPA 2015b:	+ +	(+)	÷	÷

+N: dose-response data available for neurotoxic effects, TDI or NOAEL/NOAEL

+: TDI or NOAEL/NOAEL data available, but must be more closely assessed specifically for neurotoxic effects

Exposure columns:

+: relevant exposure source

(+): exposure source might be relevant

÷ : exposure source hardly relevant

* Substances assessed for chronic neurotoxic effects in (Danish EPA 2016)

***Jensen et al. (2015) refer in their article to official ADI-values made by EFSA or WHO.*

In addition to the substances from the former Danish EPA (2016a) project, additional substances were selected here. The selection of the other ingredients in the table is made by taking into account already existing lists of neurotoxic substances produced by Grandjean and Landrigan (2006 + 2014), Giordano & Costa (2012) and the US EPA's list (see Appendix 3).

When screening and selecting the substances, emphasis has been on one or more of the following conditions:

- the substances are well established neurotoxic substances (e.g. selected in more than one of the lists)
- there is knowledge of dose-response relationships and/ or TDI, NOAEL (LOAEL) values for the neurotoxic effects
- the substances are considered relevant for this project target groups regarding relevant exposure sources
- use of existing data from the Danish EPA projects

As for the pesticides in Table 2.2, these were - besides appearing in one or several of the lists given in Appendix 3 - selected on the basis that the pesticides by Jensen et al. (2015) were found to be the most significant in terms of exposure of the Danish population, i.e. having the highest exposure in relation to their TDI values.

However, deselection has also been made of some well-known neurotoxic substances. This has happened either because they are considered not relevant to this project (methanol, ethanol, and manganese), or because it is not based on the data collected assessed to be possible to conduct a risk assessment for the substances, due to lack of more precise knowledge on the dose-response relationship and NOAEL/ LOAEL regarding their neurotoxic effects (e.g. arsenic, fluoride). The justification for the deselection is given in Appendix 3.

2.5.1 Discussion of data

In this initial screening, the substances in Table 2.2 are identified as possible candidates for subsequent exposure assessment and risk assessment.

For a number of substances in Table 2.2, tolerable exposure levels have been established regarding the substances' neurotoxic effects. This applies to substances marked * where the tolerable levels regarding chronic neurotoxic effects have been prepared in the Danish EPA (2016a) report.

Furthermore, at this stage of the project dose-response relationships/ tolerable exposure levels have been found regarding chronic neurotoxic effects for the substances acrylamide, lead and mercury. For the remaining substances, it is considered necessary to examine the data more closely regarding the neurotoxic effects before dose-response relationship and TDI/ DNEL values can be established.

More detailed assessments of the substances and conclusions regarding TDI/ DNEL values for neurotoxic effects of the substances will be made in the hazard assessment of each of the substances in Chapter 7.

3. Selection of data for exposure assessment

3.1 Strategy for collection of exposure data

Following the selection of endocrine disruptors and chronic neurotoxic substances in Chapter 2, the next step in the process towards a risk assessment of the substances is to assess whether there is sufficient exposure data for the substances, which may specify the exposure of children under 3 years and pregnant women/ unborn children.

To collect these data, the following strategy will be used for retrieving data for each substance.

Collection of data from the Danish EPA projects, such as consumer projects and LOUS assessments of the substances, and collection of data from DTU Food, the National Food Institute reports on the exposure of the Danish population through food.

Also, collection of data from the assessments by the EU scientific committees:

ECHA documents, such as RAC opinions (ECHA's Risk assessment committee), previous EU risk assessments,
EFSA (European Food Safety authority)
SCCS (EU's scientific committee for consumer safety) e.g. cosmetics
SCHER (EU's scientific committee for health and environmental risks)
SCENIHR (EU's scientific committee for newly identified health risks)

Failing adequate and updated data from these sources, additional screening will be carried out via the Internet, searching on substance names/ CAS-numbers and selected keywords to seek review articles or risk assessments of consumer related exposure to the substances.

Then, the collected literature is screened for exposure relevant data with regard to children and unborn children/ pregnant women.

For each substance and each reference, the following information is gathered in tabular form:

- reference specification
- brief description of the type of reference (e.g. expert assessment, project report, scientific article)
- brief indication of the method and description of content regarding the exposure aspects
- the specified exposure sources mentioned/ addressed and an indication of the route(s) of exposure
- which type of exposure estimates given in the source
- target groups relevant for this project
- overall assessment of the relevance of the source for further use in this project: ?, -, +, ++, +++
- specific comments relating to the reference

When assessing the relevance of the individual reference for futher use, the following criteria for the scoring were used:

+++: good and directly usable data
++: usable data, but with uncertainties or need for further calculations
+: too uncertain, but with an indication of a possible exposure

3.2 Presentation of exposure data from the literature

Appendix 4 contains all the filled exposure tables for the selected substances in Chapter 2. It should be noted that in this literature collection phase, it is the intention to make an initial assessment of whether the data are suitable for this project. A more thorough review of the most relevant literature and an evaluatation assessment of the specific exposure estimates are not included in Appendix 4, but are made in Chapter 6, where the best documented exposure estimates are selected for further risk assessment.

Thus, the tables in Appendix 4 do not necessarily contain the specific exposure values to be used, but may be included in the cases where the values are readily available during the initial screening of the reference.

Below is as an example of a print-screen image of the reviews of two of the references for acrylamide:

Acrylamide							
Reference	Type of study	Method/ content	Exposure sources; (exposure routes)	Exposure contribution from specific sources / total exposure; (mean/ worst-case)	Target groups	Relevance for exposure assessment in this project	Comments
EFSA (2015)	Expert assessment	From measured levels of acrylamide in food items in EU population exposure estimates were made based on the consumption pattern of the population. Also biomonitoring data included.	Food (oral) Especially infant food and food items based on potatoes e.g. snack, chips. For adults coffee is an important source.	Total dietary exposure: Median: Infants: 0.8-1.0 µg/kg/d Toddlers: 1.3-1.4 µg/kg/d Adults: 0.5 µg/kg/d 95-percentiles: Infant: 1.8-2.1 µg/kg/d Toddlers: 2.3-2.4 µg/kg/d Adults: 1.0 µg/kg/d	Infants, Toddlers Older children Adults	+++	Contains also hazard assessment , TDI considerations and BMDL-levels and risk assessment
DTU (2015)	Expert assessment	From measured levels of acrylamide in food items in DK population exposure estimates were made based on the consumption pattern of the population.	Food (oral) Especially in food items based on potatoes. Further, coffee, cacao, bread as important sources.	Total dietary exposure: Average (aritmetric): Children (4-14 år): 0.33 µg/kg/d Adults: 0.19 µg/kg/d 95-percentiles: Children (4-14 år): 0.89 µg/kg/d Adults: 0.46 µg/kg/d	Children (4-14 år) Adults	+++	

All references for the individual substance are reviewed and data systematised in this way. The most relevant of the references for further use for exposure calculations are highlighted (this will basically be the references scoring +++ or ++).

Below is a print-screen image regarding the overall assessment of the exposure references for acrylamide:

Overall evaluation:

EFSA (2015) and DTU (2015) together contain sufficient data for exposure assessment on acrylamide. No other significant sources than food is considered relevant to include. For drinking water the limit value of 0.1 µg acrylamide /l may be used as an upper estimate. Acrylamide has not been found in the Danish EPA's database on chemicals in consumer products.

The results from the assessments of all substances are summarised in Table 3.1 below, where the overall assessment of the data for the individual substance is listed along with the references found most suitable to provide the basis for further development of the exposure assessments for the substances.

Table 3.1 List of references considered suitable for exposure assessment

	Selected references	Assessment of references	Exposure sources	Exposure data	Comments
Acrylamide	EFSA 2015 DTU 2015	It is evaluated that EFSA (2015) and DTU (2015) contain sufficient data to estimate exposure to acrylamide. Overall, no other sources of exposure than food are expected. Acrylamide does not appear in MST's substance database for consumer products	Food Formed by food processing typically by frying potatoes, baking bread, roasting coffee	+++	There is no information regarding other sources of exposure
Aluminium	SCCS 2014 NSCFS 2013	The references provide sufficient data to estimate exposure to aluminium. Food is the primary source of exposure for infants, while cosmetics are another major source for adults.	Food (as a natural mineral) Cosmetics (eg. antiperspirant)	+++ +++	There is no information regarding other sources of exposure
BHA	EFSA 2012a	It is evaluated that EFSA (2012a) contains sufficient data to estimate exposure to BHA from food (as an additive), although data from food contact materials are missing. Data are supported by recent exposure estimates in studies by Mancini et al. (2015) and Vin et al. (2013). BHA does not appear in MST's substance database for consumer products	Food Cosmetics (additive, antioxidant)	+++ +	Any use in pharmaceuticals is not listed by EFSA (2012a). EC-SA 2015 notes that exposure from food contact materials can be problematic for children, but there does not seem to be data of exposure from food contact materials.
BHT	EFSA 2012b Danish EPA substance database	It is evaluated that EFSA (2012a) contains sufficient data to estimate exposure to BHT from food. Danish EPA's substance database for consumer products provide a number of products containing BHT, and especially content in diapers may be relevant to this project.	Food Cosmetics Other consumer products (additive, antioxidant)	+++ + + or ++	Any use in pharmaceuticals is not listed by EFSA (2012a). EFSA 2015 notes that exposure from food contact materials can be problematic for children, but there does not seem to be data of exposure from food contact materials.
Bisphenol A	EFSA 2015b Danish EPA-LOUS 2013a	It is evaluated that EFSA 2015b and Danish EPA (2011) contain sufficient data to estimate exposure to bisphenol A from food and consumer products, respectively.	Food Pacifiers Other consumer products (as residual monomer)	+++ +++ ++	
Bisphenol F	Liao 2013	Data from Liao et al. (2013) can be used to estimate exposure to bisphenol F from food (US data). Bisphenol F does not appear in the Danish EPA substance database for consumer products.	Food Paper (as residual monomer)	++ +	There are limited data on exposure to bisphenol F from food and consumer products. It is considered relevant to obtain new knowledge about exposure to bisphenol F from consumer products.
Bisphenol S	Liao 2013	Data from Liao et al. (2013) can be used to estimate exposure to bisphenol S	Food Paper	++ +	There are limited data on exposure to bisphenol S from food and con-

	Selected references	Assessment of references	Exposure sources	Exposure data	Comments
		from food (US data). Bisphenol S does not appear in the Danish EPA substance database for consumer products.	(as residual monomer)		sumer products. It is considered necessary to obtain new data knowledge about exposure to bisphenol S from consumer products. Alternatively, the substance is excluded from the project due to very insecure and low exposure values.
Lead	DTU 2015 Danish EPA-LOUS 2014f ECHA/RAC 2014 EFSA 2012d	The references listed provide sufficient data to estimate exposure to lead for children (½-3 years) and pregnant women from food and metallic articles.	Food Metallic articles	+++ +++	Accumulates in food. Migration from content in metal alloys/ objects, such as jewelry.
Brominated flame retardants: **HBCDD,** **TBBPA,** **BDE-47,** **BDE-99** **BDE-209**	DTU 2015 Danish EPA-LOUS 2014e EFSA 2011a EFSA 2011b EFSA 2011c	Accumulates in the food chain. Food and especially fish are the primary source of exposure. Data from DTU 2015 and EFSA (2011a, b, c) contain sufficient data for exposure to infants and adults through food. For exposure through dust and air, data from Danish EPA-LOUS 2014 and Harrad et al. (2006) can be used.	Food Dust Air (add to articles as flame retardants)	+++ ++ ++	
Ftalater	Danish EPA 2012a Danish EPA 2009b Bekö 2013 BfR 2011 ECHA/RAC 2016	It is evaluated that Danish EPA 2012a and Danish EPA 2009b and a number of recent publications contain sufficient data to estimate exposure for the selected phthalates in food. Data from the ECHA/ RAC 2012 regarding exposure from articles are relevant. Danish EPA 2012a, Bekö 2013 and BfR 2011 contain data for the calculation of exposure from other sources.	Food Dust Indoor air Consumer products incl. toys	+++ +++ +++ +++	Exposure is due to content in softened plastic. There are most data for DEHP, DBP, BBP, DINP and DiBP. There are limited data for the DPP, DnHP, DnOP, DHCP and DPHP. It is considered relevant to obtain new data about exposure to particular DPHP from consumer products (frequently used, but perhaps mostly outdoors and cables).
Chlorinated solvents: **Chloromethane** **Dichloromethane** **Trichloroethylene** **Tetrachloroethylene**	Danish EPA 2016a Danish EPA 2014b	Potential exposure to chloromethane, dichloromethane and trichloroethylene do not appear to be relevant for target groups of this project, thus, these substances are excluded from the project. For tetrachloroethylene, newly cleaned clothes may constitute a source of exposure.	Newly cleaned clothes / Indoor air	++	Data are considered sufficient only for tetrachloroethylene used in dry cleaning. Evaluated to be relevant for this project.

	Selected references	Assessment of references	Exposure sources	Exposure data	Comments
Hydrocarbons: **hexane** **toluene** **styrene** **and other** **C6-C12** **aliphatic and aromatic hydrocarbons**	Danish EPA 2016a Danish EPA 2016b Danish EPA -LOUS 2014b Danish EPA -LOUS 2014c Danish EPA -LOUS 2014d	The listed Danish EPA projects give sufficient data for exposure in homes and from evaporation from furniture (infant and adult). Furthermore, data from the use of consumer products containing the relevant hydrocarbons (adults).	Indoor air Consumer products (as solvents and content in fuel, such as gasoline and fuel oil)	+++ ++	
Mercury	SCENIHR 2015 DTU 2015 EFSA 2012e SCHER 2010	The references listed provide sufficient data to estimate exposure to mercury from amalgam fillings (adults), food (infants and adults) and from broken energy saving light bulbs.	Food Amalgam fillings Energy saving light bulbs	+++ +++ +++	Accumulates in food)
Nonylphenol	Danish EPA 2012a+b Gyllenhammar 2012 Danish EPA -LOUS 2013c	It is evaluated that DanishEPA 2012a contains sufficient data to estimate exposure for nonylphenol for adults. These data may be supplemented by more recent data for nonylphenol in food from Gyllenhammar 2012.	Food Dust Air Chlothes	+++ +++ +++ +++	There are no specific data for children.
Organic phosphates, flame retardants: **trichloroethyl phosphate (TCEP), tricresylphosphate (TCP), dicresylphenyl phosphate**	Danish EPA 2015d Danish EPA 2015b EU-RAR 2009 SCHER 2012 ARCADIS 2011	The primary routes of exposure for the organic phosphates are estimated to be through dust and by sucking the products and the hands that have been in contact with the products. Relevant data for exposure are missing for dicresylphenyl phosphate.	Articles, eg. baby sling Dust	++ ++	Only TCEP data is considered relevant for this project.
Paracetamol	Ersboll 2015 Ertmann 2012 Magnus 2016 Liew 2015	There are a number of Danish/ Nordic data on the use of paracetamol during pregnancy and in young children, but data require further analysis prior to use in this project.	Medicine	++/+++	.
PCB **Dioxins**	DTU 2015 DHMA 2012 EFSA 2012e Danish EPA 2014a Danish EPA 2009b Harrad et al. 2006	Food is indicated as the most significant source. For food, DTU (2015), EFSA (2012) indicate adequate data for exposure of children and adults. Data on exposure through indoor air, dust and soil are given in DHMA 2012, Danish EPA 2009 and Harrad et al. 2006.	Food Indoor air Indoor dust Soil	+++ ++/+++ ++ ++	Exposure to PCB today is due to past use, for example in sealants in construction. PCBs and dioxins accumulate in the food chain especially in fatty foods.
Pesticides	Danish EPA 2012a	It is evaluated that Danish EPA 2012a	Food	+++	It may be relevant to include expo-

	Selected references	Assessment of references	Exposure sources	Exposure data	Comments
	Jensen 2015	and Jensen et al. (2015) contain sufficient data to estimate exposure to the selected pesticides in food. For chlorpyrifos, Danish EPA 2012a performed exposure calculations also for dust.	Dust	+++ (chlorpyrifos)	sure to dust and other sources for other pesticides than chlorpyrifos, but this has a low priority in this project. There are no data for children.
PFOA **PFOS** **PFHxS**	Danish EPA 2016b DTU 2015 Danish EPA 2015a Danish EPA 2015c ECHA/RAC 2015d Danish EPA LOUS 2013b Livsmedelsverket 2013 EFSA 2012f	Food is specified as the most significant source. For food, DTU (2015), Livsmedelsverket (2013), EFSA (2013) and ECHA/ RAC (2015d) contain adequate data for exposure of children and adults. Danish EPA (2016b) indicates the exposure for children's exposure to carpets and Danish EPA (2015b) children's exposure to clothing.	Food Indoor air / dust Rugs Clothes Surface treatment / spray	+++ ++ ++ ++ +	Stain resistant and water resistant surfaces. Spray for treatment of rugs is mentioned as a possible source of exposure (no quantitative estimations given). The importance of migration from food packaging is unknown.
Propyl- and butyl paraben	SCCS 2013 Danish EPA 2012a	It is evaluated that SCCS (2012) contains sufficient data to estimate exposure for propyl- and butyl paraben. Propyl- and butyl paraben are not allowed to be used in food. The Danish EPA substance database for consumer products gives several products containing propyl- and butyl paraben, including face makeup and slimy toys.	Food Cosmetics (preservation) Other consumer products	- +++ +	Party make-up/ face colour may be relevant to examine more closely. Other Danish EPA projects have already reviewed the Danish EPA substance database for consumer products and assessed exposure in connection with projects for 2-year-old's and pregnant women's exposure to chemicals.
Siloxane D4	Danish EPA 2012a SCCS 2010 Pieri 2013	It is evaluated that Danish EPA 2012a and SCCS 2010 provide sufficient data to estimate exposure to D4 from cosmetics. Additional data on exposure to D4 from indoor air may be derived from Pieri et al. (2013).	Cosmetics Dust Indoor air	+++ + ++	Specific data for children are missing.
Triclosan	Danish EPA 2012a SCCP 2009	It is evaluated that Danish EPA 2012a and SCCP 2009 provide sufficient data to estimate exposure to triclosan from cosmetics and selected consumer and dust.	Cosmetics (preservation) Dust	+++ +++	
UV filters/ UV absorbers: **OMC** **BP-3**	Danish EPA 2012a Danish EPA 2015e	It is evaluated that Danish EPA 2012a and Danish EPA 2015 contain sufficient data to estimate exposure to BP-3 and OMC from cosmetics.	Cosmetics	+++	

3.3 Discussion of data

When going through Table 3.1, it can be seen that for most of the substances there are very good data regarding exposure via food, while data from the other sources of exposure are less extensive. This is primarily due to the wide range of relatively new EFSA assessments of the substances and the exposure estimates from DTU Food, the National Food Institute based on food analyses from the Danish food market (DTU 2015).

Regarding exposure data from **food exposure**, data for further evaluation are available for the substances:
Acrylamide, aluminium, BHA, BHT, bisphenol A/-F/-S, lead, the brominated flame retardants, phthalates, mercury, PCBs / dioxins, PFOS / PFOA / PFHxS, and pesticides

Regarding exposure data for **cosmetic products,** data are available for the substances: Aluminium, propyl and butyl paraben, siloxane D4, triclosan, and the selected UV filters. For BHA and BHT, data from the Danish Consumer Council TÆNK database may also be used.

Regarding exposure data for **indoor environment air and dust,** the references contain data for the substances:
Lead, selected brominated flame retardants, phthalates, hydrocarbons, nonylphenol, organic phosphate flame retardants (TCEP), PCB, PFOA / PFOS / PFHxS, pesticides and triclosan

For exposure through various **consumer products and articles**, data are available for the substances:
BHT, bisphenol A, selected brominated flame retardants, lead, phthalates (e.g. toys), hydrocarbons, mercury, tetrachloroethylene, nonylphenol, organic phosphate flame retardants (TCEP), PFOA / PFOS / PFHxS, propyl- and butyl paraben, and triclosan

Compared to all the substances identified in Tables 2.1 and 2.2, no relevant exposure data were found for the substances:

> *monochloromethane (methyl chloride); dichloromethane, trichloroethylene and tricresyl phosphate*

and therefore they will not be further considered in the project.

It should be noted that this overview on exposure is based on this rather the preliminary examination of the exposure data for the substances and that a somewhat different result may appear by a more elaborate review of the literature found in connection with the exposure calculations.

3.3.1 Knowledge of the exposure of the substances based on biomonitoring data

In the selection of data on biomonitoring, the emphasis is on Danish studies or studies from countries considered comparable to Denmark. Also, focus is on studies including information relevant for exposure of children and pregnant women.

Human biomonitoring data are an expression of the total exposure, to which the studied populations (or subgroups in the study) have been exposed, and thus can contribute with knowledge about the actual exposure of the individuals included in the study. Some studies have measured on different groups in the population, which in some cases can provide important knowledge about specific sources of exposure and may be usable in connection with the exposure calculations in this project.

There is great variation in the amount of relevant biomonitoring data for the various substance groups. For some substance groups, no relevant biomonitoring studies have been identified, while there for others there are several Danish studies available.

Relevant biomonitoring data are available primarily from Danish studies with calculated exposure values for the following substances:
Acrylamide, Bisphenol A, propyl- and butyl paraben, phthalates, triclosan, and OMC

For some substances, relevant biomonitoring data from Denmark are available, but without calculations on exposure levels. This applies to brominated flame-retardants, mercury, paracetamol, PCBs, pesticides, PFOS, PFOA, and BP-3.

For other substances, relevant biomonitoring data from other countries are available, however, without calculations on exposure levels. This applies to Bisphenol F, Bisphenol S, tetrachloroethylene and trichloroethylene, lead, nonyl phenol, organophosphate flame-retardants, and siloxane.

Finally, no relevant biomonitoring data have been identified for the substances:
Aluminium, BHA, BHT and the hydrocarbons.

3.4 Knowledge gaps and suggested analysis

Based on the assessment of exposure data from the literature, the following product groups are selected for chemical analysis as such measurements would be needed for further exposure assessment for the chemical substances contained in the products

A number of cosmetic products are selected to be analysed for content of the antioxidants *BHA and BHT*. For BHA and BHT, no upper limit has been established for content in cosmetics. At the same time, the Danish Consumer Council in connection with their TÆNK campaigns has collected information for 560 specific and named cosmetic products that contain BHT, and 11 products containing BHA (data given from the labelling of the products). It is therefore relatively easy to find cosmetic products containing substances for further chemical analysis. The exposure from cosmetics may especially be significant for children under 3 years and pregnant women/ unborn children in relation to leave-on products used on large parts of the body and in large quantities, such as suntan lotion, skin lotion, etc.

Pizza boxes are selected for analysis of content of bisphenol A and phthalates. Especially trays of recycled paper/ cardboard may have a potential for containing these chemicals due to the content of inks and adhesive residues in the recycled materials. The National Food Institute has in previous analyses found content of phthalates and bisphenol A in pizza boxes, and therefore a follow-up of these analyses with migration analyses is considered relevant. The substances may be able to migrate from the packaging material and into the pizza, e.g. because of contact to the hot pizza or by soaking of the cardboard with oil from the pizza. A relatively limited analysis program is evaluated to be able to achieve a good impression of the problem, as the pizza boxes on the market are considered come from relatively few producers/ importers.

Further details regarding the selection of products, test methods and test results are given in Chapter 5.

4. Regulation of the selected substances

4.1 Objective

In connection with the screening for exposure and effect data for the selected substances, it is also relevant to give an overview of the regulation of the substances. In Appendix 5, a table provides brief descriptions of the regulation of each of the substances/ substance groups in the various administrative areas related to consumer protection, i.e. in the area of:

- Chemicals regulation
- Food regulation
- Cosmetics regulation
- Toys regulation
- Biocide/pesticide regulation
- Regulation with regard to quality criteria/limit values in drinking water, soil and air
- Medicines regulation

More specifically, the table in Appendix 5 contains 7 columns indicating the status regarding:

- The EU-harmonised hazard classification of the substance in accordance with the CLP regulation (Regulation EC no. 1272/2008) Annex VI. The focus of this project is only on classifications for systemic effects (i.e. effects related to internal organs. Indications regarding classification for carcinogenic or for reproduction toxicity effects may be important as this type of classification may be due to endocrine disruption. Classification for acute toxicity (Acute tox. or STOT SE classification) or toxicity after repeated exposure (STOT RE classification) may be due to effects on the nervous system after acute or prolonged exposure.
- Whether the substance is subject to some specific restrictions on use (REACH Annex XVII) or appears on the candidate list as a SVHC substance or on the list of substances subject to authorisation (REACH Annex XIV).
- Whether the substance is regulated within the food area, e.g. whether the substance is a permitted additive, whether limit values have been set for the substance in food or migration limits for the substance in food contact materials, and whether the substance is permitted in food contact materials of plastic.
- Regulation of the substance in cosmetics, i.e. whether the substance is subject to special regulation in Annex II-VII of the cosmetics regulation.
- Regulation in toys regarding maximum content or migration limits.
- Whether the substance is covered by the biocides or pesticide regulations.
- Whether there are national or EU directive established limit values regarding the content of the substance in drinking water, soil or air.

A review of these areas for a substance will give an overview of:

- Health effects
- The sources of exposure subject to regulation of the substance.
- The sources of exposure not subject to regulation of the substance.
- Regulatory tools used for risk management of each of the substance across the administrative areas.

The medicines regulation in relation to paracetamol is carried out as a constant surveillance of the medicinal product both by national authorities (The Danish Medicines Agency, EMA) and by international authorities (The European Medicines Agency). During this surveillance, there is an on-going evaluation of the positive effects as well as the negative effects from the medicinal products.

4.2 Overview of regulation in individual areas

The regulation of the 63 substances and substance groups is summarised below. See also Appendix 5 for a more detailed description of the regulation of the individual substance.

4.2.1 Harmonised CLP classification

Information on the harmonised classification was obtained by searching for the substance on the European Chemicals Agency´s website.

CMR effects (carcinogenic, mutagenic or reproductive effects). It can be seen that 26 of the selected substance have a harmonised classification in the CLP Regulation for these effects.

Carc. classifications: 6 substances are covered which may be the result of endocrine disrupting effects (but not necessarily, as other mechanisms may result in this classification as well).

Muta. classifications cover 2 of the substances. Mutagenic classification is not in itself interesting in relation to endocrine disrupting or neurotoxic effects, but classification for mutagenicityis relevant to note, such a classification in line with classification for carcinogenicity or reproductive toxicity effects will lead to strict regulatory measures for the substances, limiting their use, e.g. in the form of banning the use in toys and cosmetics.

Repr. classifications cover 22 of the substances and may be the result of endocrine disrupting effects and/or adverse effects on neurodevelopment (but not necessarily, as other mechanisms may result in this classification as well).

STOT RE effects: this classification for *specific target organ toxicity* after repeated or prolonged exposure cover 11 of the substances. Chronic neurotoxic effects (but also other chronic effects) would cause STOT RE classification.

STOT SE and Acute Tox classification are used in case of adverse effects after single exposure and are used e.g. in connection with acute effects on the central nervous system. 5 substances are classified STOT SE, while 18 substances are classified Acute Tox.

The following of the selected suspected endocrine disruptors and chronic neurotoxic substances are subjected to harmonised classifications as Repr. Carc or STOT RE:

Harmonised classification	Substances
Repr. 1A, 1B, 2	DEHP, DBP, DIBP, BBP, dipentyl phthalate, di-n-hexyl phthalate, bisphenol A, nonylphenol, PFOA, PFOS, HBCCD, D4, mancozeb, maneb, benomyl, linuron, n-hexane, toluene, styrene, acrylamide, TCEP, lead compounds and mercury compounds
Carc. 1A, 1B, 2	PFOA, PFOS, tetrachloroethylene, acrylamide, TCEP, carbaryl, linuron
STOT RE 1, 2	PFOA, PFOS, BDE-49, BDE-99, n-hexane, toluene, styrene, white spirit, acrylamide, lead compounds, mercury compounds, linuron

The CMR classification will cause extensive restrictions on the use of the substances. All sales of chemical substances and mixtures with a harmonised CMR classification (categories 1A and 1B) are prohibited for private use and a CMR classification will cause restriction for use of the substance under several regulatory areas, for example cosmetics and toys. Restrictions on the use of CMR substances in accordance with other legislation are often linked to the harmonised classification.

As The CLP – regulation does not contain any requirements to carry out new tests for disclosing human health effects, the absence of classification for an effect may be a result of insufficient data. Thus, it should be noted that substances that are not subject to a harmonised classification still might have a potential for causing harmful effects. However, companies marketing chemical substances in the EU are obliged to assess and self-classify the substances, for effects that are not covered by a harmonised classification.

Finally, a harmonised CMR classification in categories 1A and 1B may give rise to the substances being identified as SVHC substances (Substances of Very High Concern) under the REACH regulation. This leads to the substance being included in the so-called candidate list under REACH, from which it can subsequently be included in the list of substances subject to authorisations (REACH Annex XIV). It will then be prohibited to use the substance in the EU, unless an authorisation is applied for - and granted - for a specific use in a specific period.

4.2.2 Regulation in relation to REACH

On the ECHA website it is possible to find data on individual substances and to get information whether they are Substances of Very High Concern (SVHC) and included on the candidate list , whether require authorisation prior to use (REACH Annex XIV), or whether there are specific restrictions on uses (REACH Annex XVII).

The following substances are covered by specific REACH regulation:

REACH regulation	Substances
Candidate list (SVHC-substances)	DEHP, DBP, DIBP, BBP, dipentyl phthalate, dihexyl phthalate, PFOA, HBCDD, deca-BDE, acrylamide, TCEP, some lead compounds
List of substances subject to authorisations (REACH Annex XIV)	DEHP, DBP, DIBP, BBP, HBCDD, TCEP, some lead compounds
Restrictions on use (REACH Annex XVII)	DEHP, DINP, DBP, BBP, di-n-octyl phthalate, nonylphenol, toluene, acrylamide, lead and lead compounds, mercury, bisphenol A*

*Bisphenol is from January 2020 no longer allowed in cash receipts in concentrations above 0.02 %.

Additional information regarding the type of use restrictions, see Appendix 5.

4.2.3 Regulation in the food area

In relation to the legislation on food contact materials of plastic, it was examined whether the substance is permitted for use, or whether there is a specific migration limit for release of the substance from the material. Further regulation of food contact material is, however, not included. Additionally, it was examined whether the substance is regulated by a limit value in food or whether the substance is approved as a food additive.

The following substances are covered specifically by the food regulation and the regulation on food contact material of plastic:

Regulation in the food area	Substances
Prohibited in food contact materials of plastic	dipentyl phthalate, dioctyl phthalate, dihexyl phthalate, dicyclohexyl phthalate, di-2-propyl phthalate
Allowed in food contact materials of plastic	benzophenone-1, benzophenone-3
	DEHP, DINP, DBP, BBP, bisphenol A, bisphenol S, BHA, BHT, styrene, propyl paraben, triclosan
Limit values in food	dioxins, PCBs, n-hexane, lead, mercury, and all pesticides
Allowed as food additive	BHA, BHT, aluminium

4.2.4 Regulation in the cosmetics area

Here it is examined whether the substances are covered by the cosmetics regulation, Annex II (prohibited substances in cosmetics) or whether they are subject to the general rule that CMR substances cannot not be used (unless the use has been assessed by the EU Scientific Committee on Consumer Safety and concluded as safe). Further, it is examined whether the substances are subject to specific restrictions for use in cosmetic products, for example by specifying the maximum content in the finished product (cosmetics regulation Annex III), or whether the substances are approved for use as dyes, preservatives or UV filters (cosmetics regulation Annex IV, V and VI). Finally, it is examined whether other specific rules apply (e.g. the Danish statutory order banning the use of certain parabens in cosmetic products for children under 3 years).

The following substances are covered by the cosmetics regulation:

Regulation of cosmetic products	Substances
Ban on use due to CMR classification or listed in Annex II (ban)	DEHP, DBP, DIBP, BBP, dipentyl phthalate, di-n-hexyl phthalate, bisphenol A, nonylphenol, PFOA, PFOS, HBCCD, siloxan D4, mancozeb, maneb, benomyl, linuron, n-hexane, toluene, styrene, tetrachloroethylene, acrylamide, TCEP, lead and lead compounds, mercury
Specific use restrictions/ requirements for maximum content in cosmetic products	propyl paraben, butyl paraben, benzophenone-3, OMC, toluene, mercury, aluminium, triclosan

Furthermore, there is a national Danish ban for use of propyl and butyl paraben in cosmetics intended for children under 3 years.

4.2.5 Regulation of substances in toys

Here it is examined to which extent Danish statutory orders regulate the content and migration of substances from toys.

According to the statutory order on the safety of toys (no. 13 of 10/01/2011), it is generally not permitted to use CMR substances in accessible parts of toys in concentrations that exceed the classification limit for chemical substances. Also, migration limits are set for certain substances and in addition limits are set for substances in toys for children under 3 years and toys intended to put in the mouth.

The following substances are covered by safety requirements for toys:

Regulation of toys	Substances
CMR-classification	DEHP, DBP, DIBP, BBP, dipentyl phthalate, di-n-hexyl phthalate, bisphenol A, nonylphenol, PFOA, PFOS,

	HBCCD, D4, mancozeb, maneb, benomyl, linuron, n-hexane, toluene, styrene, acrylamide, TCEP, lead compounds, mercury compounds, tetrachloroethylene, acrylamide, carbaryl
Limit value for content	DEHP**, DINP**, DBP**, DIBP*, BBP**, dipentyl phthalate*, dihexyl phthalate*, dioctyl phthalate**, dicyclohexyl phthalate*, di-2-propylhexyl phthalate*, TCEP
Migration limits	lead, mercury, aluminium, bisphenol A

* These phthalates are covered by the Danish Executive Order on ban of phthalates in toys and childcare articles

**These phthalates are covered by REACH Annex XVII

4.2.6 Regulation, biocides/ pesticides

The following substances are approved in connection with the use as a biocide/ pesticide or under review as a biocide:

Biocide/ Pesticide	Substances
Approved for specific biocide use in the EU, or under review	some aluminium compounds
Approved as a pesticide in the EU	aluminium-phosphide, pirimiphos-methyl, mancozeb, maneb, propineb, dimethoat, linuron, methomyl
Available as a pesticide on the Danish market	aluminium-phosphide, mancozeb and maneb.

4.2.7 Regulation, limit values

The substances have also been examined for the existence of limit values or quality criteria for content in drinking water, soil and air. The limit values and the quality criteria found are recommended values set by the Danish Environmental Protection Agency (C-values in air, evaporation criteria for e.g. indoor environment, quality criteria for soil and water), or values set by Danish statutory orders issued for drinking water quality or outdoor air quality.

For the following substances, quality criteria/ limit values have been found in drinking water, soil or air:

Quality criteria	Substances
Drinking water	DEHP, sum of phthalates except DEHP (in this project relevant for DINP, DBP, DIBP, BBP dipentyl phthalate, dihexyl phthalate, dioctyl phthalate, dicyclohexyl phthalate, di-2-propyl phthalate), nonylphenol, phenols (such as BHA, BHT and bisphenol A), pesticide on general, C_9-alkylbenzenes, styrene, acrylamide, tetrachloroethylene, lead, mercury, aluminium, PFOS and PFOA (included in the sum criterion for PFAS)
Soil	DEHP, sum of phthalates except DEHP (relevant for DINP, DBP, DIBP, BBP, dipentyl phthalate, dihexyl phthalate, dioctyl phthalate, dicyclohexyl phthalate, di-2-propyl phthalate), nonylphenol, PFOS and PFOA (included in the sum criterion for PFAS), phenols (such as BHA, BHT), volatile hydrocarbons, tetrachloroethylene, lead (inorganic), mercury (inorganic)
Air	DEHP, other phthalates except DEHP, nonylphenol, BHT, n-hexane, heptane, toluene, xylene, styrene, white spirit, C_9-aromatics, ethylbenzene, tetrachloroethylene, acrylamide, lead, mercury, aluminium

4.2.8 Regulation, medicines

As part of the medicines regulation there is an on-going evaluation regarding positive as well as negative effects from the medicinal products. This applies to all approved medicinal products with the aim to keep under surveillance the safety in all relevant populations including children and pregnant women.

Regulation of medicines	Substances
Medicinal product approved and surveilled by the Danish Medicines Agency and EMA	Paracetamol

4.2.9 Overall assessment

By looking over the different regulatory areas, it is noted that many of the substances are relatively well regulated across the areas. Regulation within many areas can be an indication that there is (– or has been for some time) considerable focus on the substance because of its harmful effects, and that it has been the objective to limit the exposure on a broad scale. A regulation across areas may also be an indication for potential exposure occurring from many sources due to widespread use (or previous use) of the substance and its possible spread via consumer goods and through the environment. This is known e.g. from metals (lead) and some phthalates, which have been/ are widely used in many different areas and where the exposure is thus spread out on many sources.

5. Analysis of selected substances in selected products

5.1 Background for selection of substances and product types

As indicated in Section 3.4, it was decided that it would be appropriate in this project to focus on the following two areas regarding the selection of products for chemical analyses:

- Selection and analysis of pizza boxes for migration of bisphenols (A, S, and F) and phthalates, which may be present in recycled cardboard due to the presence in e.g. inks.
- Selection and analysis of cosmetic products for the presence of BHT and BHA.

5.2 Identification and purchase of specific products

There has not been an actual survey of the two areas (pizza boxes from recycled cardboard and cosmetic products containing BHT/ BHA), but the two areas were studied based on previous studies/ reports.

5.2.1 Pizza boxes

Pizza boxes made of recycled cardboard may contain residues of phthalates and bisphenols from ink and glue. The National Food Institute has analysed this in a previous project (The Danish Veterinary and Food Administration, 2010), where they found a few phthalates and bisphenol A in the extract from some (recycled) paper/ cardboard, primarily pizza boxes and cardboard packaging for pasta. They assessed, based on the results from this project, that the content of the phthalate DIBP in cardboard packaging for pasta was of concern, as it could represent up to 70 % of the tolerable intake. This was on the assumption that a pregnant woman daily consumes 150 grams of pasta packaged in recycled cardboard and the total content of DIBP in the package would migrate into the food (pasta). There were no migration analyses of phthalates and bisphenol A into food, but only an extraction (corresponding to a total content, as the extraction was performed with 95 % ethanol).

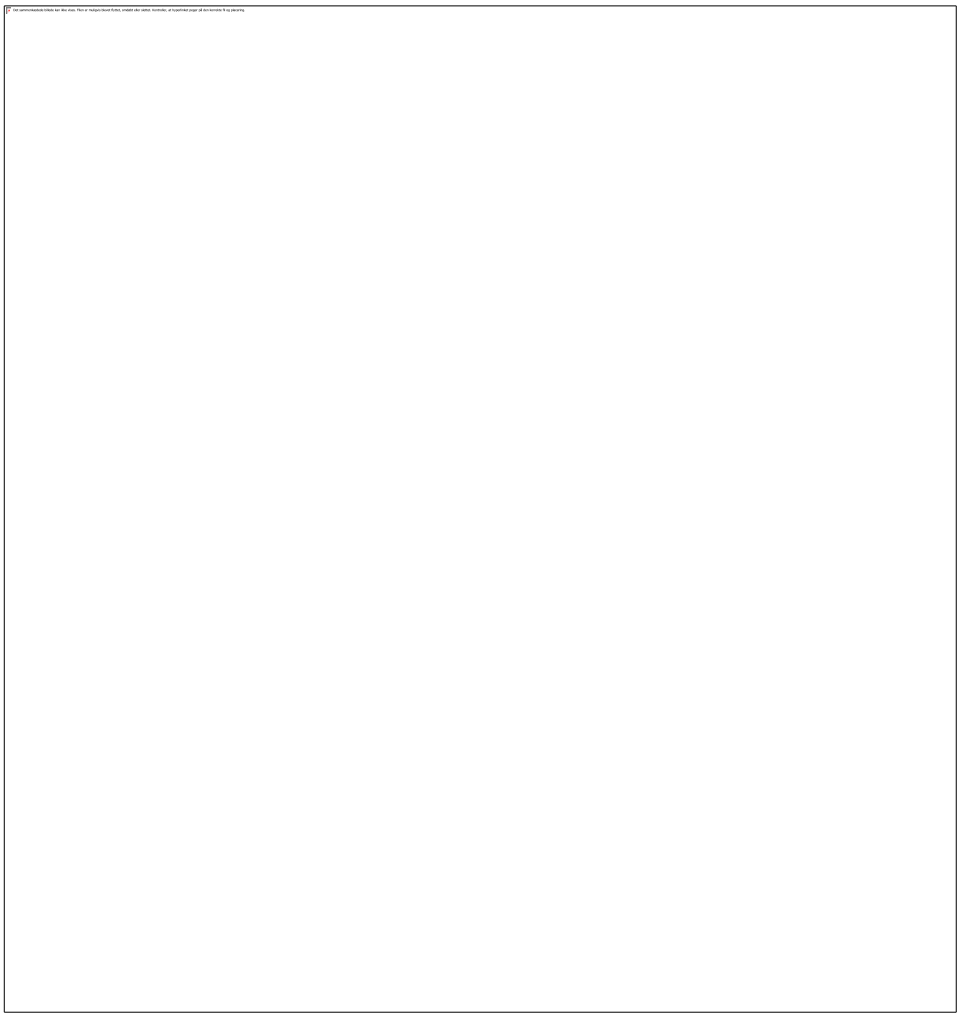
In this project, it was decided only to analyse the migration of phthalates and bisphenols from pizza boxes, as the exposure from cardboard for pasta (primarily lasagna sheets) is estimated to be minimal.

Initially, two distributors of pizza boxes on the Danish market were contacted. These distributors were identified by an Internet search. Both of these distributors of pizza boxes described that the majority of pizza boxes on the Danish market consist of recycled cardboard, but that the recycled cardboard is present in the core of the pizza box. The part of the pizza box that comes into contact with food is made of new paper/ cardboard.

To identify the most used pizza boxes on the Danish market, FORCE Technology created a small internal questionnaire survey that was sent out to employees of FORCE Technology Denmark. This means that the potential participants in the study were scattered around the country; however, with most of the potential participants in the metropolitan area. The small questionnaire survey included one question and was created in SurveyMonkey. The question was "Which pizza box does your local pizzeria use? Which pizza boxes do you recognise?".

There were 10 possible answers, of which 9 answers consisted of 9 different images of pizza boxes identified via an Internet search and from the two suppliers of pizza boxes initially contacted. The last possible answer was "None of the above. You can describe the box in the field below".
There were 176 answers with a total of 325 pizza boxes, i.e. on average each person indicated that they could recognise 1.8 pizza boxes. The distribution of answers on the individual pizza boxes is indicated in Figure 5.1 below.

Figure 5.1 Distribution of answer rate for the various pizza boxes



Based on this small questionnaire survey and contact with suppliers of pizza boxes, 4 pizza boxes were purchased for analysis. These 4 pizza boxes were 4 out of the 6 pizza boxes frequently recognised by FORCE Technology's employees from their local pizzeria, and which according to the supplier of pizza boxes originate from different manufacturers. Pizza boxes no. 1 and 2, which according to this small survey seem to be far the most used pizza boxes, were both selected for analysis. One of the major suppliers of pizza boxes that was contacted described that the boxes come from different pizza box manufacturers in Italy and represent a wide range of the quality on the market.
In addition, one additional of the most frequently used pizza boxes was purchased from a local pizzeria. Here a brown pizza box was deliberately chosen, as several of FORCE Technology's employees commented on this in the comments field. However, it is not known whether this pizza box originates from the same manufacturer as the other purchased pizza boxes.
In total, 3 white pizza boxes and 2 brown pizza boxes were purchased. All 5 pizza boxes consist of recycled cardboard according to information from the supplier and/ or described on the

pizza box. Furthermore, all 5 pizza boxes had printing on both the front and back of the pizza box. The printing on the front side of the pizza boxes in all five cases takes up a very large part of the front of the box. For all pizza boxes, it applies that there is no printing inside the pizza box, where the food is in contact with the box.

5.2.2 Cosmetic products

BHT and BHA are used as antioxidants in cosmetic products, which is the application described for the substances in the CosIng database. There are no established limit values for the use of BHA and BHT in cosmetics, but the responsible person for the cosmetic product shall prepare a safety/ risk assessment of the product's content, including the content of BHT and BHA.

The Danish newspaper "Politiken" writes in an article from January 2016[1] that creams may contain BHT. The project team contacted TÆNK at the Danish Consumer Council to check whether there are cosmetic products with content of BHT and/ or BHA in the TÆNK (Think) database from the app "Kemiluppen". TÆNK's database "Kemiluppen" contains 6707 different cosmetic products (contact to TÆNK in June 2016). A search via TÆNK's database "Kemiluppen" (performed by TÆNK in June 2016) shows that 560 different scanned products contain BHT and 11 products contain BHA, as well as 5 products that contain both BHA and BHT. Thus, 8.3 % of the scanned cosmetic products contained BHT and 0.16 % contained BHA. BHT is far more common than BHA - at least among the products scanned via TÆNK's app.

It was therefore decided that products containing BHT and BHA had to be purchased based on the lists received from TÆNK of cosmetic products containing these two antioxidants.

The TÆNK database indicates the number of times the app has been used by the consumers and a product has been scanned. The number of scans can be an indication of how widespread the use of the product is. The products with BHA have between 65 and 1962 scans per product. The products with BHT have between 1 and 6175 scans per product.

Detailed examination have been made of the extracts that TÆNK forwarded on products containing BHT and BHA. The review of the products shows that the following types of products may contain BHT and BHA (number of products within each category is indicated in brackets) - see Table 5.1 and Table 5.2.

Table 5.1 Product groups containing BHT according to TÆNK's database "Kemiluppen"
(product groups indicated in **bold** are considered the most interesting from an exposure point of view)

• Cleansing / makeup remover / wash (8)	• Hair wax (8)
• **Aftersun (2)**	• Intimate care (1)
• **Baby lotion/cream (1)**	• Lip balm (34)
• Conditioner / conditioning treatment (15)	• Lipstick/lipgloss (3)
• Razor (38)	• Mascara (5)
• Shaving cream / shaving gel (23)	• Mask (2)
• BB/CC cream (9)	• **Oil, e.g. body oil (10)**
• **Body lotion / body cream (61)***	• Perfume / eau de toilette (7)
• Body shampoo/body gel/foam bath (24)	• Primer (1)
• Concealer / corrector (2)	• Powder (9)
• **Cream / lotion / serum (40)***	• Ointment / gel (1)
• **Deodorant (156)**	• Scrub / peeling (2)

[1] http://politiken.dk/forbrugogliv/sundhedogmotion/forbrugerkemi/ECE3016352/milde-cremer-kan-indeholde-skadelig-kemi/

• Malesticks) (1) • Foot care (1) • Foundation (12) • Gift boxes for children (perfumes?) (1) • Gift boxes for teens / adults (6) • Hand care (7) • Hand soap solid (7) • Hand soap liquid (3) • Hair dye (1) • Hair spray/ heat spray (3) • Hair oil / cream/ lotion (5) • Hair foam (1)	• Self tanning (1) • Shampoo (15) • Skin tonic / toner / mist (3) • **Sunscreen/ sun lotion / sun gel (7)** • **Sun spray (7)** • Sun stick (1) • Toothpaste (1) • Theatre makeup (4) • Eye cream (3) • Eye makeup remover (2) • Eye shadow (2)

It should be noted that the difference between the product groups "body lotion/body cream" and "cream/lotion/serum" (marked with *) appears to be the latter category primarily including face creams.

Table 5.2 Product groups containing BHA according to TÆNK's database "Kemiluppen"
(product groups indicated in **bold** are considered the most interesting from an exposure point of view)

• Hair oil/cream/lotion (1) • Hair foam (1) • Hair wax (1) • Lip balm (1)	• Lipstick/lipgloss (1) • **Oil (2)** • Powder (3) • Oinment/gel (1)

In theory, women may use several different products in the course of a day, all of which may contain BHT and/ or BHA, but it was decided to focus on the products applied to the largest area of the skin, and which at the same time are leave-on products (products marked in **bold**). In cooperation with the Danish EPA, it was decided to purchase cosmetic products based on the lists from TÆNK's database and the following criteria:

1. Only products with high exposure, i.e. leave-on products, were selected. Primarily whole body products were selected, such as body lotions, body oils, suntan lotions and products for the face. I.e. the products marked with **bold** in Table 5.1 and Table 5.2.
2. Products from the product groups with many products containing BHT or BHA were primarily purchased, as it indicates that the use of BHT or BHA is relatively common in these product groups. However, one baby lotion/ cream were more specifically selected, as this is a cream (according to TÆNK) recommended for small children with eczema.
3. Products from different manufacturers were selected for each product group, so that not several products from the same maufacturer are analysed within the same product group. However, in some cases both a body oil and a body lotion from the same manufacturer were purchased.
4. Products within the above criteria with the largest number of scans in "Kemiluppen" were mainly selected, i.e. more individuals seem to use these products (although it should be taken only as an expression of frequent scanning by the consumers that uses the app "Kemiluppen").
5. Both cheap and expensive products were purchased.
6. A total of 24 products was purchased in the following categories:
   - 10 body lotions
   - 3 body oil products (one product contains both BHA and BHT)
   - 4 face creams
   - 3 sunscreen/ aftersun
   - 4 deodorants (roll-on)
7. The products were purchased only if BHT or BHA still appeared from the declaration of contents.

The contents of BHT and BHA were determined quantitatively in the cosmetic products. There were no migration analyses, as it is assumed that the entire contents of BHT and BHA, respectively, are in contact with the skin.

It should be noted that for some body lotions, but especially for sunscreen/ aftersun products, it turned out that the products selected for purchase no longer contained BHT. Manufacturers typically prepare new formulations of sunscreens every year, and several manufacturers have chosen to formulate these without BHT. These products were not purchased, and other products containing BHT were selected instead. For this reason, it was decided to purchase an excess of body lotions, as many products from different manufacturers are still identified with content of BHT from this product group, and as this product group was the second largest product group containing BHT (based on TÆNK's database).

It should also be noted that TÆNK's database seems to contain an excess of more expensive cosmetics. Therefore, also cheaper (supermarket) products were purchased that appeared from TÆNK's database - even though they may not have the highest number of scans - and further 1-2 products (containing BHT) were purchased from the supermarket, even though they did not appear from TÆNK's database. The distribution of price and manufacturer for the different purchased cosmetic products are listed in Table 5.3 below.

Table 5.1 Overview of the distribution of products in product group, manufacturer and price

Lab. no.	Manufacturer no.	Price (DKK)	Price (DKK) /100 mL	Comments
BO1	P1	194.95	97	
BO2	P2	81.93	137	Recommended especially for prevention of stretch marks (pregnant women)
BO3	P3	30	20	
BL1	P1	184.95	92	Recommended especially for children (eczema skin)
BL2	P4	249	125	
BL3	P5	290	145	
BL4	P6	235	118	
BL5	P7	199	50	
BL6	P8	225	90	
BL7	P9	35	11	
BL8	P3	38	15	
BL9	P11	126	50	Recommended especially for babys
BL10	P21	59	39	
FC1	P10	253.95	508	
FC2	P11	69.95	140	
FC3	P12	585	1950	
FC4	P13	495	990	
SS1	P14	89.25	45	
SS2	P15	255	204	
SS3	P16	150	75	
DEO1	P17	12	24	
DEO2	P18	12	24	
DEO3	P19	kr. 180	360	
DEO4	P20	kr. 195	260	

BO = Body oil, BL = Body lotion, FC = Face cream, SS = Sunscreen/After sun,
DEO = deodorant (roll-on)

5.3 Selection and description of analyses

This section describes the analytical methods selected for the analyses of pizza boxes (migration of phthalates and bisphenols) and cosmetic products (content of BHT and BHA).

5.3.1 Pizza boxes

Choice of analytical method

Choice of analytical method for the pizza boxes was discussed before initiation. The issue with pizza boxes and migration of components to the food is the lack of guidelines for how to make these analyses. Methods have been established for the migration of substances from plastic materials in contact with food, but not for goods of paper and cardboard. It is possible to apply methods for plastic products in contact with food as a starting point, but unlike plastic cardboard/ paper products typically disintegrate (divides in the different layers of paper during disintegration), when making migration analyses for food. The migration analyses therefore resemble a total extraction (i.e. content determination) rather than determining which substances actually migrate into the food.

The previous analysis of phthalates and bisphenol A in pizza boxes made by the Danish Veterinary and Food Administration (2010) was performed as an extraction in 95 % ethanol, where the pizza box was cut into small pieces and boiled in ethanol for 1 hour. This is in fact a content determination rather than a migration.

There is no specific legislation for food contact materials of cardboard and paper, and therefore no established test conditions for migration to cardboard and paper. According to Commission Regulation no. 10/2011 (EU Regulation 10, 2011) for plastic materials in contact with food, the following food simulants are established (Table 2 in Appendix III) relevant for the foods "sandwiches, toasted bread, pizza and the like containing foods of any kind", depending on whether there are fatty substances on the surface or not:

For food products with a lipophilic content on the surface:
- Food simulant A – 10 % ethanol (for food with hydrophilic properties)
- Food simulant D2 – vegetable oil (for food with lipophilic properties)

For other food products:
- Food simulant E – Tenax (for dry food)

Furthermore, it is stated in the regulation that the food simulant D1 (ethanol 50 %) is used for food with oil-in-water emulsions, as is the case for pizza toppings.

There is no specific usable food simulant, but several different ones depending on the surface of the food. In case of pizza, the crust is dry food where Tenax seems as the most proper food simulant, whereas the pizza filling often consists of a mixture of aqueous (tomatoes) and fatty (cheese, oil) fillings. However, if the pizza is cut in the pizzeria, the oil/ aqueous liquid may leak into the cardboard so that it is no longer a dry surface.

An aspect of choosing oil or ethanol food simulants is that the cardboard from the pizza box, which is cut and placed in the simulant, will most likely disintegrate into the different layers of paper in the solvent, whereby there will be no real migration analysis, but rather an extraction of the contents. The food simulant Tenax is a dry simulant in powder form and is therefore suitable to simulate dry food properties. Tenax is also the only food simulant that can simulate a unilateral migration, i.e. simulating what is actually released from the pizza box via the gas phase and physical contact with the food.

It was decided to carry out migration (or more specifically testing of the content in the material) on all pizza boxes for food simulant D1 consisting of 50 % ethanol solution as a simulator for oil-in-water emulsions, as pizza fillings often consist of both aqueous fillings and oily fillings at the same time, which may leak into the cardboard by cutting. This migration analysis will be a worst-case migration, as the cardboard is expected to disintegrate into the different layers of paper in the solution. In addition, it was decided to make migration to Tenax for the two pizza boxes, for the greatest release to the ethanol simulator was identified, in order to examine if phthalates and bisphenols are actually released from a pizza box into the food.

The migration conditions are selected in cooperation with the Danish Veterinary and Food Administration and the National Food Institute, DTU Food to 70 °C for 1 hour. The conditions are selected based on the view that this temperature is the average temperature of food from a hot oven (200 °C) to eating temperature. The migration condition of 1 hour is selected as the most realistic time from the pizza is placed in a box until it is consumed - despite the fact that a standard test from the plastic regulation (EU Regulation 10, 2011) indicates 2 hours at 70 °C. There is no standard test conditions from the plastic regulation that fit perfectly to the example of bringing hot pizza from the oven home in a pizza box.

Description of the analytical method

Two different migration analyses are made:

1. Migration of Bisphenol A, F, S and phthalates from pizza boxes to liquid simulant (50 % ethanol) at 70 °C for 1 hour.
2. Migration of Bisphenol A, F, S and phthalates from pizza boxes to solid phase simulant (Tenax) at 70 °C for 1 hour.

Migration to liquid simulant (50 % ethanol)
Migration to 50 % ethanol water is measured.

A piece of cardboard from a pizza box (with no ink) having an area of 5 cm^2 on each side and thus a total of 10 cm^2 is placed in a glass bottle with a screw cap and added the migration *liquid*. The bottle is placed in a 70 °C hot oven for 1 hour. After cooling, the liquid is decanted and used for further analysis. Pieces from pizza boxes with no ink were deliberately chosen, as the pizza under normal conditions is not in contact with the ink that is only on the outside of pizza boxes.

Duplicate analyses were performed on all pizza boxes for each type of analysis. Moreover, a standard addition was performed that has been added a known amount of selected substance to a sample and verified with a known amount of selected substances, without cardboard.

Phthalate analysis: The migration liquid is transferred to a separating funnel, internal standard and diluted hydrochloric acid are added, and then shaken with dichloromethane. The dichloromethane phase is separated, dried with sodium sulfate and analysed on GCMS for the specified phthalates.

Bisphenol analysis: The migration liquid is evaporated to dryness in vacuum oven at 50 °C. The residue is dissolved in acetonitrile. As bisphenol S, contrary to expectations, could not be analysed on the GCMS, nor as trimethylsilyl derivative (TMS derivative), the solution was analysed by HPLC-UV. Bisphenol A and bisphenol F are measured at 230 and 280 nm, and bisphenol S at 257 nm. Unfortunately, the cardboard released interfering substances, especially with respect to bisphenol A. Bisphenol A and bisphenol F can be analysed by GCMS, where there is no interference. The results are shown in Table 5.4.

Migration to solid phase simulant (Tenax)
The two selected pizza boxes (PIZ4 and PIZ5), in which the phthalates are identified in the greatest quantities in the analysis using ethanol, and in which there are simultaneously measured the highest value for bisphenol A (only this value measured above the detection limit) were analysed in accordance with DIN EN 14338. 1 dm^2 cardboard is covered with 4 g of polyphenylene oxide (Tenax) and heated to 70 °C in a cabinet for 1 hour to simulate migration from the cardboard into a pizza. Then, Tenax is extracted with solvent and the extract is analysed on GCMS for content of phthalates and bisphenol A (bisphenol F can be identified by the same method as bisphenol A and is thus also examined for, although it was not identified above the detection limit in the ethanol analysis). Bisphenol S was not identified above the detection limit in the analysis of ethanol and was therefore not further analysed here. The results are shown in Table 5.5.

GC/MS conditions
A 30 meter, 0.25 mm in diameter, 0,25 µm DB5 MS column is used for analysis.

- Injector temp.: 325 °C
- Flow: 1 ml/min.
- Injection: pulsed/splitless mode 2 min. and then 50 ml/min.
- Temperature ion source: 200 °C and transfer line: 250 °C
- Oven: 60 °C, hold 0.5 min., 45 °C/min. up to 150 °C, 15 °C /min. to 300 °C, hold 7.5 min.
- SIR for the specific ions

Retrieval of DIBP and DEHP in the control sample is 110 % and retrieval of DIBP and DEHP at standard addition (addition of 4 µg of each phthalate to samples corresponding to 40 µg/ dm^2) is between 95-110 %.

Retrieval of bisphenol A by the standard addition (addition of 4 µg bisphenol A to samples, corresponding to in the sample) is between 80 and 120 %. Retrieval of bisphenol S from standard addition is 80 %.

Quantification limit for DINP is 25 µg/dm^2 (DINP consists of several individual substances measured in total) and for the other phthalates, the quantitation limit is between 1 and 3 µg/dm^2 (see results in Table 5.4). The analysis uncertainty is 30 % relative to all measured substances. The quantification limit for bisphenol A by HPLC is 15 µg/dm^2 due to interference, and 5 µg/dm^2 for bisphenol F and bisphenol S. The quantification limit is 3 times higher than the detection limit where a substance can be seen in trace amount, but cannot be quantified.

5.3.2 Cosmetic products

Choice of analytical method

For determination of BHT and BHA content in cosmetic products, an analytical method was selected that is usable for various cosmetic products.

Description of analytical method

A purification of the sample is made where oils and water are held back and the analytes are extracted. Duplicate determinations were carried out of samples, controls, blind and standard addition to selected samples was made to check the method performance. Calibration was done using external calibration on specific ions for the two substances. By means of mass spectra and retention time, the substances could be identified.

Sample preparation

0.1 g of sample is weighed and mixed with sodium sulfate and Florisil. It is then extracted with ethyl acetate and turbid samples are filtered through a 0.45 µm PTFE syringe filter prior to analysis.

GC/MS conditions

A 30 meter, 0.25 mm in diameter, 0,25 µm DB5 MS column is used for analysis.

- Injector temp.: 325 °C
- Flow: 1 ml/min.
- Injection: pulsed/splitless mode 2 min. and then 50 ml/min.
- Temperature ion source: 200 °C and transfer line: 250 °C
- Oven: 60 °C, hold 1 min., 10 °C/min. up to 140 °C, hold 2 min., 10 °C /min. to 180 °C, 15 °C to 320 °C
- MS-scan: 45 – 310 m/z from 4 min. till end and SIR for the ions 165 m/z (BHA) and 205 m/z (BHT)

Retrieval of BHA in the control sample is 99 % and retrieval of BHA at standard addition (addition of 10 µg BHA to samples, corresponding to 0.01 % in the sample) is between 101-113 %. Retrieval of BHT in the control sample is 88 % and retrieval of BHT at standard addition (addition of 10 ug BHT to samples, corresponding to 0.01 % in the sample) is between 89-105 %. Quantification limit for BHA and BHT is 0.0002 % and the analytical uncertainty is 30 % relative. The quantification limit is 3 times greater than the detection limit where a substance can be seen in trace amount, but cannot be quantified. An analytical uncertainty of 30 % is considered normal at these low levels.

5.4 Analytical results

The analytical results of migration analyses of pizza boxes and determination of the contents of BHT and BHA in cosmetic products are listed below.

5.4.1 Pizza boxes

It should be noted that, as expected, the pizza box cardboard separated in the individual paper layers (virgin paper, recycled paper and virgin paper) in the migration liquid (50 % ethanol). The results from the migration to 50 % ethanol should therefore be seen as worst-case results as a pizza will not under normal circumstances be in contact with the inner layer of recycled cardboard.

The results of the analyses are presented in Table 5.4 and Table 5.5 below. Note that duplicate determinations of the analyses have been made, and therefore the analytical results are an expression of the average of the two analytical results for the individual products. The relative standard deviation for the duplicate determinations is between 1 and 14 %.

Pizza boxes nos. 3 and 5 are brown pizza boxes, the remaining three pizza boxes are white.

Analyses have been made for the following bisphenols and phthalates (which are among the selected substances (see Table 2.1)):

- Bisphenols
    - Bisphenol A – CAS 80-05-7
    - Bisphenol S – CAS 80-09-1
    - Bisphenol F – CAS 620-92-8
- Phthalates
    - DEHP (di-ethyl-hexyl-phthalate) – CAS 117-81-7
    - DINP (di-iso-nonyl-phthalate) – CAS 28553-12-0
    - DIBP (di-iso-butyl-phthalate) – CAS 84-69-5
    - DBP (di-butyl-phthalate) – CAS 84-74-2
    - BBP (butyl-benzyl-phthalate) – CAS 85-68-7
    - DPP (dipentyl phthalate) – CAS 131-18-0
    - DnHP (di-n-hexyl phthalate) – CAS 84-75-3
    - DnOP (di-n-octyl phthalate) – CAS 117-84-0
    - DCHP (dicyclohexyl phthalate) – CAS 84-61-7
    - DPHP (bis(2-propylheptyl) phthalate) – CAS 53306-54-0

Table 5.2 Overview of analytical results for migration to 50 % ethanol

Substance name	PIZ1 (white)	PIZ2 (white)	PIZ3 (brown)	PIZ4 (white)	PIZ5 (brown)
	(µg/dm^2)	(µg/dm^2)	(µg/dm^2)	(µg/dm^2)	(µg/dm^2)
Bisphenol A	19	18	29	38	34
Bisphenol S	< 5	< 5	< 5	< 5	< 5
Bisphenol F	< 5	< 5	< 5	< 5	< 5
DEHP	19.9	< 2	14.9	24.7	31.0
DINP	34.3	< 25	32.7	35.0	35.8
DIBP	11.9	< 1	2.6	10.1	11.5
DBP	4.7	< 1	3.7	5.5	7.4
BBP	3.4	< 1	< 1	2.0	2.9
DPP	< 2	< 1	< 1	< 2	< 2
DnHP	< 3	< 3	< 3	< 3	< 3

Substance name	PIZ1 (white)	PIZ2 (white)	PIZ3 (brown)	PIZ4 (white)	PIZ5 (brown)
DnOP	3.8	< 1	3.8	3.8	4.2
DCHP	< 3	< 3	< 3	< 3	< 3
DPHP	< 3	< 3	< 3	< 3	< 3

PIZ = Pizza box

From pizza boxes nos. 1, 3, 4 and 5, the phthalates DEHP, DINP, DIBP, DBP and DnOP have been identified in approximately identical amounts in the migration liquid. BBP was also identified in the migration liquid from pizza boxes 1, 4, and 5. The highest values were identified in pizza box no. 5. Bisphenol A was the only bisphenol that could be detected in the migration liquid. For pizza boxes nos. 4 and 5, higher values of bisphenol A have been identified in the migration liquid than for the other pizza boxes.

Based on these analytical results, pizza boxes nos. 4 and 5 were selected for migration to the solid phase simulant (Tenax). The results are given in Table 5.5 below. It can be seen that neither phthalates nor bisphenols were identified for migration to Tenax under the conditions mentioned.

Table 5.3 Overview of analytical results for migration to solid phase simulant (Tenax)

Substance name	PIZ4	PIZ5
	(µg/dm^2)	(µg/dm^2)
Bisphenol A	<10	<10
Bisphenol F	<10	<10
DEHP	<5	<5
DINP	<50*	<50*
DIBP	<5	<5
DBP	<5	<5
BBP	<10**	<10**
DPP	<5	<5
DnHP	<5	<5
DnOP	<5	<5
DCHP	<5	<5
DPHP	<5	<5

PIZ = Pizza box

* The detection limit for DINP is much higher than for the other phthalates, as this is a mixed phthalate. About 35 µg/dm^2 was observed by the liquid migration to ethanol in the two pizza boxes.

** The detection limit for BBP is higher than for the others, but BBP above 5 µg/dm^2 by liquid migration to ethanol was not observed.

5.4.2 Cosmetic products

The results of the analyses are given in Table 5.6 (BHT) and Table 5.7 (BHA) below. Note that duplicate determinations of the analyses have been made, and therefore the analytical results reflect the average of the two analytical results for the individual products.

Table 5.4 Overview of analytical results for content of BHT in the cosmetic products

Lab. no.	Content of BHT (weight %)	Relative standard deviation (%)
BO1	0.0029	7.2
BO2	0.064	14.4
BO3	0.0099	14.3
BL1	0.023[2]	7.7
BL2	< 0.0002	
BL3	0.18	7.2
BL4	0.23	12.8
BL5	0.057	1.6
BL6	0.13	7.2
BL7	0.11	9.6
BL8	0.0002	0.6
BL9	0.069	6.9
BL10	0.11	2.8
FC1	0.22	1.0
FC2	0.0071	4.5
FC3	0.10	2.9
FC4	0.0078	15.5
SS1	0.32	5.5
SS2	0.0009	14.7
SS3	0.0017	2.5
DEO1	0.11	3.5
DEO2	0.056	3.9
DEO3	0.052	5.9
DEO4	0.23	5.2

BO = Body oil, BL = Body lotion, FC = Face cream,
SS = Sunscreen/After sun, DEO = deodorant (roll-on)

The identified highest concentration of BHT is 0.32 % (3200 ppm) in a sunscreen (SS1) and the identified lowest concentration is 0.0002 % (2 ppm) in a body lotion (BL8). In BL2 no content of BHT was identified (or levels above the detection limit of 0.0002 %), despite the fact that it was apparent from the declaration of contents.

Table 5.5 Overview of analytical results for content of BHA in the cosmetic products

Lab. no.	Content of BHA (weight-%)	Relative standard deviation (%)
BO1	0.0039	11.0

BO = Body oil

[2] The producer of this product has informed us that the measured result is not consistent with their own internal analysis resulting in a content of BHT of 0.0094

Only one product - a body oil (BO1) – contained BHA in a concentration of 0.0039 % (39 ppm). For the remaining products, a content of BHA above the detection limit of 2 ppm was not identified - but these cosmetic products had no declared content of BHA.

6. Exposure assessments

6.1 Method

In connection with exposure assessments for the selected substances, this chapter further evaluates the data sources from Chapter 3, where relevant literature for more detailed exposure assessment was identified. The objective is to estimate the exposure for the individual sources of exposure to the substances for children under 3 years and pregnant women/ unborn children.
The starting point for setting up scenarios and establish exposure estimates is a more detailed review of the designated literature in Appendix 4 and Table 3.1, i.e. literature that scored either ++ or +++, and possibly make a further review of the data referred to in these sources.

As the work includes detailed review of the designated literature for about 60 substances, it has been necessary to set up a table matrix for assessing data and for selecting the most relevant exposure values. Processing and evaluation of data are described in the Appendices 6a, 6b and 6c.

Appendix 6a includes assessment of data for the exposure of small children (under 3 years) to the selected substances, while Appendix 6b deals with the assessment of data for the exposure of pregnant women/ unborn children. Appendix 6c includes collection of biomonitoring data for the substances.

The exposure tables in Appendices 6a and 6b (see these) are constructed with six columns for systematisation of data, where

- the first column indicates the literature used
- the second column indicates the sources of exposure
- the third column indicates the identified exposure values
- the fourth column indicates further explanations or modification of data
- the fifth column indicates mean exposure values, or what is indicated to be typical exposure
- the sixth column indicates 95-percentile exposure, or what is indicated to be a realistic worst-case exposure

Furthermore, the fifth and sixth columns indicate, whether the specified exposure has been calculated as an external dosage (by oral or dermal exposure or by inhalation), or whether the dose is indicated as an internal dose (i.e. the dose absorbed by the body).

In addition, for each substance there is a field for assessing the overall exposure from multiple sources simultaneously, a field for commenting the data, and a field for specifying the relevant biomonitoring data and their significance.

For some substances, different exposure estimates for a specific source are indicated, and in these cases, it is assessed which data are the most relevant for Danish conditions. The exposure values in the table indicated in **bold** style are the values that will be used in the risk assessment of the substance in Chapter 8.

For certain substances that is well-known in connection with the contamination of groundwater/ drinking water and soil (e.g. lead), exposure in connection with the content of the substance in these media is indicated, and contents similar to the Danish limit values/ quality criteria are used as a basis for the exposure assessment.

Food and drinking water
For the majority of the selected substances, for which exposure data have been found, food exposure represents the most significant source of exposure. This is due to the fact that many of the substances for several years have been in the focus of the food authorities in the EU, and therefore a number of substances have been covered by monitoring programs for the content in food items (e.g. lead, mercury, methyl mercury, brominated compounds (PBDEs), perfluorinated compounds (PFOA, PFAS), dioxin, PCBs, bisphenol A, acrylamide and pesticides).

For all these substances, it applies that relatively updated estimates of the population's exposure are available partly from assessments from EFSA (European Food Safety Authority) and partly from Danish assessments from the National Food Institute. The estimates are usually given as typical average exposure levels (e.g. median values) or as high exposure (e.g. a 95-percentile), which usually will provide a relatively solid basis for a risk assessment.

The hallmark of food exposure is that this will cause exposure of the entire population to a greater or lesser extent, which means that a risk assessment based on food exposure will be relatively comprehensive for the population and in some cases also for specific subgroups (groups of different ages or groups with different types of food consumption). So in the cases where for example a 95-percentile is used as high exposure in the report, this can be regarded as a highly realistic worst-case situation as 5 % of the population (or the subgroup covered by the estimate) will in principle be exposed at higher levels.

When calculating exposure estimates from the analysed contents in various food items and based on assumptions about population groups' intake of these food items, it is inevitable that uncertainties to a greater or lesser extent will be associated with these estimates, depending on the extent of the data material, and how representative it is. For substances having good biomarkers of exposure (e.g. lead and acrylamide), and where the food is the dominant source, it is often valuable to complement exposure data with biomonitoring data for the current target groups.

Indoor environment/ outdoor environment
There are rarely as systematic analyses of the exposure from indoor environment and the outdoor environment as from food. Apart from a few substances, for which many data exist for content in the indoor environment (e.g. lead, phthalates) and content in soil (e.g. lead), the data are often very scattered, and it can be difficult to assess how representative the data are. Thus, estimates of indoor/ outdoor environment exposure must be used with great caution. This applies to the estimated contributions in this report on e.g. brominated, chlorinated and perfluorinated substances where the knowledge for contributions through these sources is typically very limited.

Finally, the contribution from the indoor environment is very variable as it depends on age of the building, used building materials, any restorations, the type of furniture selected, and not least the activities that take place indoors. Especially hobby activities and use of chemical products could affect the indoor environment to a great extent.

Cosmetics

For cosmetics, just as for foods, it applies that use/ consumption of these products lead to exposure to all components in the products. Knowledge of contents in a cosmetic product and knowledge of a typical or high consumption pattern would thus give a fairly accurate indication of the exposure of the individual consumer. The degree of public exposure will to a greater extent than food exposure be preference determined, as the use of cosmetics varies greatly in the population: some may not use other cosmetics than toothpaste and soap/ shampoo, while others have a high consumption of various cosmetic products. Finally, exposure varies greatly depending on the type of cosmetic product, as there will be relatively low exposure to products that are washed away (e.g. a rinse off product as shampoo) or when using small amounts (e.g. eyeliner), while the exposure will be high for leave-on products such as body lotion or sun-screen used in relatively large amounts when used.

In this project, the exposure estimates for substances contained in cosmetics are therefore calculated either from the recommended use amounts (e.g. sunscreen) or from exposure values used in expert assessments, which typically are based on the guidelines for exposure assessment in SCCS's guidance on risk assessment of cosmetics.

Most cosmetic products are applied to the skin, and here values for the skin penetration rate and systemic uptake of the substance is crucial parameter to know for any risk assessment for endocrine disrupting and neurotoxic substances. Precisely this aspect is crucial for risk assessment of e.g. aluminium, where there is a lack of knowledge about the absorption through skin.

Consumer products

As for cosmetics, the exposure of the individual consumer regarding consumer products is preference determined, i.e. which products are purchased and used and in which way. The estimates included in the exposure estimates are largely based on assumptions, as exposure estimation for consumer products is substantially less standardised than for e.g. foods and cosmetics where some standard value/ default values apply for various type of products. Often, considerably more assumptions are included in the assessment of consumer products, and each assumption may be subject to some uncertainty. E.g., for many consumer articles the amount of a substance emitted from the product is of great importance, for example, by migration from a solid matrix, which may be very variable depending of the different conditions and thus very difficult to estimate (e.g. how much lead migrates from lead-containing articles in contact with skin or by sucking of metallic objects).

As exposure assessment for consumer products is very product specific, the contributions to exposure via consumer products (e.g. toys or textiles) are in most cases performed as separate or special scenarios in this project.

6.2 Exposure assessments, children under 3 years

In the summary Tables 6.1 - 6.4 the exposure is separated as far as possible into the various exposure sources:

- food + drinking water
- indoor environment + outdoor environment (soil)
- cosmetics
- other consumer products/ articles

Further, a single medicinal product, paracetamol is included in the column of consumer products.

In connection with the exposure values the exposure routes is indicated: oral (o); dermal (d), inhalation (inh) or the value is given as internal (int) value as the systemic dose; i.e. the dose that has been absorbed in connection with the external exposure. If “int” is not indicated in connection to a value, the reference that is used for the value has not specifically addressed the exposure value as an internal value. When “-“ is indicated in the tables indicates that no data for the source has been found, or if the potential exposure is considered very low/ insignificant in comparison with the other exposure sources given for the substance. “?” indicates that exposure cannot be ruled out but the magnitude of this is unknown.

By calculation of aggregated exposure, the exposure estimates are added for the sources food+ drinking water; indoor + outdoor environment; cosmetics and consumer products. Some special scenarios, however, are kept separate and indicated as a specific scenario in the tables. These scenarios may be very rare scenarios occurring at special occasions or absolute worst case scenarios and therefore not considered suitable for a more general aggregated exposure estimate. (e.g. mercury exposure in relation to a broken energy saving light bulb under worst-case exposure conditions; DEHP exposure from use of plastic sandals with feet smeared with sun lotion; use of baby sling with very high TCEP content). Here it is considered most relevant to calculate the aggregated exposure without contribution from these scenarios and to assess these specific scenarios on their own.

Tables 6.1 and 6.2 contain a summary of the results of exposure estimates from Appendix 6a for children under 3 years for the endocrine disruptors (Table 6.1) and chronic neurotoxic substances (Table 6.2).

Table 6.1 Exposure table for endocrine disruptors, medium, high and scenario-specific exposure to children under 3 years

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment /soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Antioxidants						
BHA, medium	230 (o)	-		-	230 (o)	No data
BHA, high	570 (o)	-		-	570 (o)	No data
BHT, medium	91(o)	-	480 (derm) corresponding 19.2 (int)	-	111 (int)	No data
BHT, high	300 (o, int)	1 (o, int)	2016 (derm) corresponding 81 (int)	-	382 (int)	No data
Brominated substances						
HBCDD, medium	0.0011 (o)	0.0059 (o)	-	?	0.007 (o)	No data
HBCDD, high dust exp.	0.0027 (o)	0.33 (o)	-	?	0.333 (o)	No data
TBBPA, medium	?	-	-	?	?	No data
TBBPA, specific scenario	0.0557 (o)	0.0046 (o)	-	?	0.060 (o)	No data
Deca-BDE, medium	0.010 (o)	0.0005 (o)	-	?	0.011 (o)	No data
Deca-BDE, specific scenario	0.018 (o)	0.080 (o)	-	?	0.098 (o)	No data
Chlorinated substances						
PCBtotal (as PCB6), medium	0.0126 (o)	-	-	?	0.0126 (o)	PCB7, breast milk: 999 ng/kg/d (o)
PCBtotal (as PCB6), high incl. contaminated indoor environm.	0.0236 (o)	0.300 (inh) 0.015 (o)			0.0236 (o) + 0.300 (inh) + 0.015 (o)*	PCB7 (max, breast milk): 2733 ng/kg/d (o)
DL-PCB, medium	2.12 pg TCDD eqv/kg/d (o)	-	-	-	2.12 pg TCDD eqv/kg/d (o)	
DL-PCBs, high	4.6 pg TCDD eqv/kg/d (o)	?	-	-	4.6 pg TCDD eqv/kg/d (o)	
Fluorinated substances						

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment /soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
PFOA, medium	0.00326 (o)	0.00038 (o+inh)	-	?	0.0036 (o+inh)	No data
PFOA, high	0.00484 (o)	0.00083 (o+inh)	-	?	0.0057 (o)	No data
PFOA, specific scenario	0.014 (o)	-	-	?	0.014 (o)	No data
PFOS, medium	0.00131 (o)	0.0001 (o+inh)	-	?	0.0014 (o+inh)	0.02 µg/kg bw/d Breast milk
PFOS, high	0.00339 (o)	0.00039 (o+inh)	-	?	0.0038 (o+inh)	-
PFOS, specific scenario	0.013 (o)	-	-	?	0.013 (o)	0.054 µg/kg bw/d Breast milk
PFHxS, medium	0.00016 (o)	-	-	?	0.00016 (o)	No data
PFHxS, high	0.00024 (o)	-	-	?	0.00024 (o)	No data
Phthalates						
DEHP, medium	4.66 (int)	4.22 (int)	?	3.49 (int)	12.37 (int)	4.77 µg/kg/d
DEHP, high	7.09 (int)	21.85 (int)	?	27.32 (int)	56.26 (int)	19.7 µg/kg/d
DBP, medium	0.7 (int)	0.28 (int)	?	1.2 (int)	2.18 (int)	3.56 µg/kg/d
DBP, high	1.24 (int)	1.47 (int)	?	9.22 (int)	11.93 (int)	13.06 µg/kg/d
DIBP, medium	1.03	0.27 (int)	?	1.06 (int)	2.37 (int)	3.19 µg/kg/d
DIBP, high	9.2 (int)	1.41 (int)	?	8.16 (int)	18.59 (int)	16.06 µg/kg/d
BBP, medium	0.0	0.08 (int)	?	0.31 (int)	0.39 (int)	0.49 µg/kg/d
BBP, high	0.0	0.42 (int)	?	2.43 (int)	2.85 (int)	2.90 µg/kg/d
DINP, medium	2.3 (int) aggregated expsoure (biomonitoring)				2.3 (int)	2.3 µg/kg bw/d
DINP, high	9.1 (int) aggregated expsoure (biomonitoring)				9.1 (int)	9.1 µg/kg bw/d
DnOP, medium	0.04 (int)	?	?	?	0.04 (int)	No data
DnOP, high	0.35 (int)	?	?	?	0.35 (int)	No data
DCHP, medium	0.106 (int)	?	?	?	0.106 (int)	No data
DCHP, high	0.383 (int)	?	?	?	0.383 (int)	No data
DPHP, medium	0.10 (int)	?	?	?	0.10 (int)	No data

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment /soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
DPHP, high	0.26 (int)	?	?	?	0.26 (int)	No data
DPHP, specific scenario toys	0	0	0	135 (int)	135 (int)	No data
Medicine						
Paracetamol, medium	-	-	-	12 500 (o)	12 500 (o)	No data
Paracetamol, specific scenario	-	-	-	50 000 (o)	50 000 (o)	No data
Parabens						
PB+BB, medium	-	-	19 (int)	?	19 (int)	Propylparaben: 301.3 ng/kg bw/d
PB+BB, specific scenario	-	-	59 (int)	?	59 (int)	Propylparaben: 381.1 ng/kg bw/d
Phenols						
Bisphenol A, medium	0.375 (o. int)	0.012 (int) sum of indoor env., cosmetics and consumer products			0.387 (int)	0.04-0.066 µg/kg bw/d (median)
Bisphenol A, high	0.857 (o. int)	0.021 (int) sum of indoor env., cosmetics and consumer products			0.878 (int)	0.15-0.283 µg/kg bw/d (high)
Bisphenol A, specific scenario, pacifier	-	-	-	0.230 (o)	-	-
Bisphenol F, medium	0.0223 (o)	?	?	?	0.0223 (o)	No data
Bisphenol F, high	0.0703 (o)	?	?	?	0.0703 (o)	No data
Bisphenol S, medium	0.0043 (o)	?	?	?	0.0043 (o)	No data
Bisphenol S, high	0.0047 (o)	?	?	?	0.0047 (o)	No data
Nonylphenol, medium	0.6 (o. int)	0.19 (o, int)	-	-	0.79 (int)	No data
Nonylphenol, specific scenario	1.6 (o. int)	0.375 (o, int)	-	-	1.98 (int)	No data
Pesticider						
Diazinone, medium	0.011 (o)	-	-	-	0.011 (o)	No data
Pirimiphos-methyl, medium	0.10 (o)	-	-	-	0.10 (o)	No data

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment /soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Procymidone, medium	0.043 (o)	-	-	-	0.043 (o)	No data
Dithiocarbamates, medium	0.50 (o)	-	-	-	0.50 (o)	No data
Linuron, medium	0.024 (o)	-	-	-	0.024 (o)	No data
UV-filters						
BP-3, medium	-	-	1700(int)	-	1700 (int)	0.027 µg/kg bw/d,
BP-3, specific scenario	-	-	3300 (int)	-	3300 (int)	high: 1.388 µg/kg bw/d
OMC, medium	-	-	1400 (int)	-	1400 (int)	No data
OMC, specific scenario	-	-	2800 (int)	-	2800 (int)	No data
Other substances						
Siloxane D4, medium	No data					No data
Siloxane D4, specific scenario	No data					
Triclosan, medium	?	7.7 (o)	-)	?	7.7 (o)	No data on children
Triclosan, specific scenario	?	30 (o)	-	?	30 (o)	No data on children

( ) : indicates that the dose is by oral ingestion (o), dermal exposure (derm), inhalation (inh), or the dose is calculated as internal dose (int)

- : no data, probably relatively poor

? : possible exposure of unknown size (on the existing basis data are missing, any further data will require more in-depth literature search and evaluation)

* for PCBtotal only data from dust is used for calculations of RCR values for hormone disrupting effects in chapter 8, as it was not possible to derive a suitable DNEL for PCB total in indoor air and food, see chapter 7

Medium: indicates a typical exposure level, an average exposure or a median value

High: indicates a high but realistic exposure level, for example, expressed by a 95-percentile

Specific scenario: indicates a particular individual scenario typically with very high exposure

From Appendix 6a, it is further apparent that from the literature found (or lack thereof) it was not possible to make exposure estimates for *dipentyl phthalate* and *di-n-hexyl phthalate* for children under 3 years, and therefore these substances are not carried forword to risk assessment in this project.

Table 6.2 Exposure table for neurotoxic substances, medium, high and scenario-specific exposure to children under 3 years

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment/ soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Brominated substances						
HBCDD, medium	0.0011 (o)	0.0059 (o)	-	?	0.007 (o)	No data
HBCDD, high dust exp.	0.0027 (o)	0.330 (o)	-	?	0.333 (o)	No data
TBBPA, medium	?	0.001 (o)	-	?	?	No data
TBBPA, specific scenario	0.056 (o)	0.0046 (o)	-	?	0.060 (o)	No data
Deca-BDE, medium	0.010 (o)	0.0005 (o)	-	?	0.011 (o)	No data
Deca-BDE, specific scenario	0.018 (o)	0.080 (o)	-	?	0.098 (o)	No data
Tetra-BDE-47, medium	0.018 (o)	?	--	?	0.018 (o)	0.009 µg/kg/d
Tetra-BDE-47, specific scenario	0.070 (o)	?	-	?	0.070 (o)	0.1 µg/kg/d
Penta-BDE-99, medium	0.007 (o)	?	-	?	0.007 (o)	0.003 µg/kg/d
Penta-BDE-99, specific scenario	0.026 (o)	?	-	?	0.026 (o)	0.043 µg/kg/d
Chlorinated substances						
PCBtotal (as PCB6), medium	0.0126 (o)	-	-	-	0.0126 (o)	PCB7 in breast milk: 0.999 µg/kg/d (o)
PCBtotal (asPCB6), specific scenario	0.0236 (o)	0.015 (o) 0.300 (inh)			0.039 (o) 0.300 (inh)	PCB7 in breast milk: 2.733 µg/kg/d (o)
PCB, dioxinlike + dioxins, medium	2.1 pg TCDD-eqv. /kg/d (o)	-	-	-	2.1 pg TCDD-eqv. /kg/d (o)	No data
PCB, dioxinlike + dioxins, high	4.6 pg TCDD-eqv. /kg/d (o)	-	-	-	4.6 pg TCDD-eqv. /kg/d (o)	No data
Tetrachlorethylen, medium	-	3 µg/m^3	-	-	3 µg/m^3	No data
Tetrachlorethylen, specific scenario	-	100 µg/m^3	-	Dry-cleaned clothes, evaporation indoors	100 µg/m^3	No data
TCEP, medium	0.01 (o)	1.7 (o+inh)	-	12 (d)	13.8 (o+d+inh)	No data

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment/ soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
TCEP, specific scenario (baby sling)	-	-	-	72.5 (int)		No data
Fluorerede stoffer						
PFOA, medium	0.00326 (o)	0.00038 (o+inh)	-	?	0.0036 (o+inh)	No data
PFOA, high	0.00484 (o)	0.00083 (o+inh)	-	?	0.0057 (o)	No data
PFOA, specific scenario	0.014 (o)	-	-	?	0.014 (o)	No data
PFOS, medium	0.00131 (o)	0.0001 (o+inh)	-	?	0.0014 (o+inh)	0.02 µg/kg bw/d
PFOS, high	0.00339 (o)	0.00039 (o+inh)	-	?	0.0038 (o+inh)	-
PFOS, specific scenario	0.013 (o)	-	-	?	0.013 (o)	0.054 µg/kg bw/d
PFHxS, medium	0.00016 (o)	-	-	?	0.00016 (o)	No data
PFHxS, high	0.00024 (o)	-	-	?	0.00024 (o)	No data
Hydrocarbons						
Toluene, medium	-	9.1 µg/m^3 (inh)	-	-	9.1 µg/m^3 (inh)	No data
Toluene, high	-	55.3 µg/m^3 (inh)	-	-	55.3 µg/m^3 (inh)	No data
Toluene, specific scenario	-	230 µg/m^3 (inh)	-	-	230 µg/m^3 (inh)	No data
Xylenes, medium	-	7.5 µg/m^3 (inh)	-	-	7.5 µg/m^3 (inh)	No data
Xylenes, high	-	42.3 µg/m^3 (inh)	-	-	42.3 µg/m^3 (inh)	No data
Xylenes, specific scenario	-	146 µg/m^3 (inh)	-	-	146 µg/m^3 (inh)	No data
Ethylbenzene, medium	-	3.2 µg/m^3 (inh)	-	-	3.2 µg/m^3 (inh)	No data
Ethylbenzene, high	-	8.2 µg/m^3 (inh)	-	-	8.2 µg/m^3 (inh)	No data
Ethylbenzene, specific scenario	-	230 µg/m^3 (inh)	-	-	230 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, medium	-	79 µg/m^3 (inh)	-	-	79 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, high	-	232 µg/m^3 (inh)	-	-	232 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, specific scenario indoors	-	1500 µg/m^3 (inh)	-	-	1500 µg/m^3 (inh)	No data
Styrene, medium	-	-	-	-	-	No data

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment/ soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Styrene, high	-	2.5 µg/m^3 (inh)	-	-	2.5 µg/m^3 (inh)	No data
Metals						
Aluminium, medium	0.136 (int)	-	-	-	0.136 (int)	No data
Aluminium, high.	0.286 (int)	-	-	-	0.286 (int)	No data
Lead, medium	1.21 (o)	0.9 (o)	-	0.45 (o)	2.56 (o)	No data
Lead, specific scenario	3.36 (o)	3.6 (o)	-	4.6 (o)	11.6 (o)	No data
Mercury, inorg. medium	0.19 (o)	-	-	-	0.19 (o)	No data
Mercury,inorg. high	0.31 (o)	-	-	-	0.31 (o)	No data
Mercury, inorg. specific scenario (broken energy bulb)				10 (int)	10 (int)	No data
Methyl mercury, medium	0.039 (o)	-	-	-	0.039 (o)	No data
Methyl mercury, high	0.23 (o)	-	-	-	0.23 (o)	No data
Pesticides (only medium estimates available)						
Diazinone, medium	0.011 (o)	-	-	-	0.011 (o)	No data
Dimethoate, medium	0.015 (o)	-	-	-	0.015 (o)	No data
Chlorfenvinphos, medium	0.0066 (o)	-	-	-	0.0066 (o)	No data
Methamidophos, medium	0.0069 (o)	-	-	-	0.0069(o)	No data
Oxydemeton-methyl (sum), medium	0.0018 (o)	-	-	-	0.0018 (o)	No data
Carbaryl, medium	0.10 (o)	-	-	-	0.10 (o)	No data
Carbendazim and benomyl, medium	0.20 (o)	-	-	-	0.20 (o)	No data
Methomyl and thiodicarb, medium	0.020 (o)	-	-	-	0.020 (o)	No data
Phenols						
Bisphenol A, medium	0.375 (o)		0.012 (o)		0.387 (o, int)	0.04-0.066 µg/kg bw/d
Bisphenol A, specific scenario	0.857 (o)		0.021 (o)		0.878 (o, int)	0.15-0.283 µg/kg bw/d

Substance	Foods + drinking water µg/kg/d	Indoor environment + Outdoor environment/ soil µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Bisphenol A, specific scenario by use of pacifier				0.230 (o)	0.230 (o)	
Other substances						
Acrylamide, medium	1.4 (o)	-	-	-	1.4 (o)	0.54 µg/kg bw/d
Acrylamide, high	2.4 (o)	-	-	-	2.4 (o)	1.91 µg/kg bw/d

( ) : indicates that dose is by oral intake (○), dermal exposure (derm), inhalation (inh), or the dose is calculated as internal dose (int)

- : no data, probably relatively poor

? : possible exposure of unknown size (on the existing basis data are missing, additional data will require more in-depth literature search and assessment)

Medium: indicates a typical exposure level, an average exposure or a median value

High: indicates a high but realistic exposure level, for example, expressed by a 95-percentile

Specific scenario: indicates a particular individual scenario typically with very high exposure

6.3 Exposure assessments, pregnant women/ unborn children

Similarly, exposure estimates prepared for pregnant / unborn child. Below are the results of exposure estimates from Appendix 6b for women indicated for the endocrine disruptors (Table 6.3) and for the chronic neurotoxic substances (Table 6.4).

Table 6.3 Exposure table for endocrine disruptors, medium, high and scenario-specific exposure of pregnant women/ unborn children

Substance	Foods + drink-ing water µg/kg/d	Indoor environment µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Antioxidants						
BHA, medium	130 (o)	-		-	130 (o)	No data
BHA, high	1140 (o)	-		-	1140 (o)	No data
BHT, medium	30 (o, int)	-	300 (derm) or 12 (int)	-	42 (int)	No data
BHT, specific scenario	210 (o, int)	-	1260 (derm) or 50.4 (int)	-	260 (int)	No data
Brominated substances						
HBCDD, medium	0.0002 (o)	?	-	?	0.0002 (o)	No data
HBCDD, high, high dust exp.	0.0008 (o)	?	-	?	0.0008 (o)	No data
TBBPA, medium	?	-	-	?	?	No data
TBBPA, specific scenario	0.0026 (o)	-	-	?	0.0026 (o)	No data
Deca-BDE, medium	0.003 (o)	(o)	-	?	0.003 (o)	No data
Deca-BDE, specific scenario	0.005 (o)	(o)	-	?	0.005 (o)	No data
Chlorinated substances						
PCBtotal (as PCB6), medium	0.0063 (o)	-	-	?	0.0063 (o)*	No data on adults
PCBtotal (as PCB6), high incl. contaminated indoor environm.	0.0118 (o)	0.2 (inh)	-	?	0.0118 (o)*	No data on adults
DL-PCB+ dioxins, medium	1.06 pg TCDD eqv/kg/d (o)			?	1.06 pg TCDD eqv/kg/d (o)	No data
DL-PCBs, high	2.3 pg TCDD eqv/kg/d (o)	-	-	-	2.3 pg TCDD eqv/kg/d (o)	No data
Fluorinated substances						
PFOA, medium	0.00057 (o)	0.00002 (o+inh)	-	?	0.00059 (o+inh)	No data
PFOA, high	0.00086 (o)	0.000084 (o+inh)	-	?	0.00094 (o+inh)	No data
PFOA, specific scenario	0.0061 (o)	0.0061 (o)	Ingen data			

PFOS, medium	0.00045 (o)	0.000018 (o+inh)	-	?	0.00047 (o)	No data on adults
PFOS, high	0.00115 (o)	0.00008 (o+inh)	-	?	0.00123(o)	No data on adults
PFOS, specific scenario	0.0068 (o)	-	-	-	0.0068 (o)	No data on adults
PFHxS, medium	0.00003 (o)	-	-	?	0.00003 (o)	No data
PFHxS, high	0.00005 (o)	-	-	?	0.00005 (o)	No data
Phthalates						
DEHP, medium	1.49 (int)	0.48 (int)	?	2.12 (int)	4.09 (int)	1.56 µg/kg/d
DEHP, high	7.63 (int)	2.52 (int)	?	7.63 (int)	13.01 (int)	5.12 µg/kg/d
DEHP, specific scenario, plastic sandal				24.2 (int)	24.2 (int)	
DBP, medium	0.08 (int)	0.02 (int)	?	0.74 (int)	0.84 (int)	0.543 µg/kg/d
DBP, high	0.16 (int)	0.12 (int)	?	2.56 (int)	2.92 (int)	1.34 µg/kg/d
DIBP, medium	0.14 (int)	0.02 (int)	?	0.65 (int)	0.82 (int)	1.66 µg/kg/d
DIBP, high	0.28 (int)	0.11 (int)	?	2.34 (int)	2.74 (int)	3.04 µg/kg/d
DIBP, specifikt scenarie, plastik-sandal				13.5 (int)	13.5 (int)	-
BBP, medium	0.05 (int)	0.01 (int)	?	0.19 (int)	0.25 (int)	0.13 µg/kg/d
BBP, high	0.12 (int)	0.03 (int)	?	0.68 (int)	0.83 (int)	0.47 µg/kg/d
DINP, medium	0.45 (int)	0.017 (int)			0.47 (int)	0.75 µg/kg/d
DINP, high	1.4 (int)	0.8 (int)			2.20 (int)	5.50 µg/kg/d
DnOP, medium	0.022 (int)				0.022 (int)	No data
DnOP, high	0.063 (int)				0.063 (int)	No data
DCHP, medium	0.016 (int)				0.016 (int)	No data
DCHP, high	0.031 (int)				0.031 (int)	No data
Medicine						
Paracetamol, medium	-	-	-	16 670 (o)	16 670 (o)	No data
Paracetamol, specific scenario	-	-	-	66 670 (o)	66 670 (o)	No data
Parabens						
PB+BB, medium	-	-	3.8 (int)	?	3.8 (int)	No data on adults

PB+BB, specific scenario	-	-	16 (int)	?	16 (int)	No data on adults
Pesticides						
Diazinon, medium	0.0055 (o)	-	-	-	0.0055 (o)	No data
Diazinon, high	0.0086 (o)	-	-	-	0.0086 (o)	No data
Pirimiphos-methyl, medium	0.050 (o)	-	-	-	0.050 (o)	No data
Pirimiphos-methyl, high	0.079 (o)	-	-	-	0.079 (o)	No data
Procymidone, medium	0.021 (o)	-	-	-	0.021 (o)	No data
Procymidone, high	0.033 (o)	-	-	-	0.033 (o)	No data
Dithiocarbamates, medium	0.24 (o)	-	-	-	0.24 (o)	No data
Dithiocarbamates, high	0.39 (o)	-	-	-	0.39 (o)	No data
Linuron, medium	0.012 (o)	-	-	-	0.012 (o)	No data
Linuron, high	0.018 (o)	-	-	-	0.018 (o)	No data
Phenols						
Bisphenol A, medium	0.132 (o. int)	0.084 (int) sum of indoor environment, cosmetics, articles			0.216 (o, int)	0.03-0.04 µg/kg bw/d
Bisphenol A, high	0.388 (o. int)	0.678 (int) sum of indoor environment, cosmetics, articles			1.066 (o, int)	high: 0.13-0.24 µg/kg bw/d
Bisphenol A, worst-case, cash receipts	-	-	-	0.260 (int)	0.260 (int)	-
Bisphenol F, medium	0.0075 (o)	?	?	?	0.0075 (o)	No data
Bisphenol F, high	0.0197 (o)	?	?	?	0.0197 (o)	No data
Bisphenol S, medium	0.0013 (o)	?	?	?	0.0013 (o)	No data
Bisphenol S, high	0.0017 (o)	?	?	?	0.0017 (o)	No data
Nonylphenol, medium	0.48 (o. int)	0.0277 (inh. o, int)	-	4.53 (d, int)	4.8 (int)	No data
Nonylphenol, worst-case	1.03 (o. int)	0.1057 (inh. o, int)	-	9.05 (d, int)	10.2 (int)	No data
UV-filters						
BP-3, medium	-		720 (int)	-	720 (int)	No data on adults
BP-3, high	-	-	1400 (int)	-	1400 (int)	No data on adults
OMC, medium	-	-	600 (int)	-	600 (int)	No data

OMC, high	-	-	1200 (int)	-	1200 (int)	No data
Other substances						
Siloxane D4, medium			0.003 (int)		0.003 (int)	No data
Siloxane D4, high			20.4 (int)		20.4 (int)	No data
Triclosan, medium	-	0.0015 (o)	7.3 (o)	-	7.3 (o)	0.49 µg/kg bw/d
Triclosan, high	-	-	22.0 (o)	-	22.0 (o)	90-perc: 0.565 µg/kg bw/d

( ) : indicates that the dose is by oral ingestion (o), dermal exposure (d), inhalational exposure (inh), or the dose is calculated as internal dose (int)

- : no data, probably relatively poor

? : possible exposure of unknown size (on the existing basis data are missing, additional data will require more in-depth literature search and assessment)

* for PCBtotal the data is not used for the estimation of RCR values for hormone disruption effects (Chapter 8), as it was not possible to derive a suitable DNEL for PCB in indoor air and food, see (see Chapter 7).

Medium: indicates a typical exposure level, an average exposure or a median value

High: indicates a high but realistic exposure level, for example, expressed by a 95-percentile

Specific scenario: indicates a particular individual scenario typically with very high exposure

From Appendix 6b, it is further apparent that from the literature found (or lack thereof) it was not possible to make exposure estimates for *dipentyl phthalate, di-n-hexyl phthalate* and di-2-propylheptyl phthalate (DPHP) for pregnant women/ unborn children, and therefore these substances are not carried forword to risk assessment in this project.

Table 6.4 Exposure table for neurotoxic substances, *medium, high and scenario-specific* exposure of pregnant women/ unborn children

Substance	Foods + drinking water µg/kg/d	Indoor environment µg/kg/d	Cosmetics µg/kg/d	Consumer products µg/kg/d	Aggregated exposure µg/kg/d	Human biomonitoring data
Brominated substances						
HBCDD, medium	0.0002 (o)	-	-	?	0.0002 (o)	No data
HBCDD, high, high dust exp.	0.0008 (o)	-	-	?	0.0008 (o)	No data
TBBPA, medium	?	-	-	?	?	No data
TBBPA, high	0.0026 (o)	-	-	?	0.0026 (o)	No data
Deca-BDE, medium	0.003 (o)	-	-	?	0.003 (o)	No data
Deca-BDE, high	0.005 (o)	-	-	?	0.005 (o)	No data
Tetra-BDE-47, medium	0.002 (o)	?	--	?	0.002 (o)	No data on adults
Tetra-BDE-47, high	0.007 (o)	?	-	?	0.007 (o)	No data on adults
Penta-BDE-99, medium	0.0007 (o)	?	-	?	0.0007 (o)	No data on adults
Penta-BDE-99, high	0.0014 (o)	?	-	?	0.0014 (o)	No data on adults
Chlorinated substances						
PCBtotal (as PCB6), medium	0.0063 (o)	-	-	-	0.0063 (o)	No data on adults
PCBtotal (as PCB6), high	0.0118 (o)	0.200 (inh)	-	-	0.0118 (o) 0.200 (inh)	No data on adults
PCB, dioxin like + dioxins, medium	1.06 pg TCDD-eqv. /kg/d (o)	-	-	-	1.06 pg TCDD-eqv. /kg/d (o)	No data
PCB, dioxin like + dioxins, high	2.3 pg TCDD-eqv./kg/d (o)	-	-	-	2.3 pg TCDD-eqv. /kg/d (o)	No data
Tetrachloroethylene, medium	-	3 µg/m^3	-	-	3 µg/m^3	No data
Tetrachloroethylene, specific scenario Indoors	-	100 µg/m^3	-	Dry-cleaned clothes, evaporation indoors	100 µg/m^3	No data
Tetrachloroethylene, specific scenario When wearing dry-cleaned clothes	-	-	-	767 (d+inh)	767 (d+inh)	No data

TCEP, medium	-	-	-	?	-	No data
TCEP, specific scenario (baby sling)	-	-	-	4.5 (d+o=int)	4.5 (int)	No data
Fluorinated substances						
PFOA, medium	0.00057 (o)	0.000022 (o+inh)	-	?	0.00059 (o+inh)	No data
PFOA, high	0.00086 (o)	0.000084 (o+inh)	-	?	0.00094 (o)	No data
PFOA, specific scenario	0.0061 (o)	0.000018 (o+inh)	-	?	0.0061 (o)	No data
PFOS, medium	0.00045 (o)	0.000018 (o+inh)	-	?	0.00047 (o+inh)	No data on adults
PFOS, high	0.00115 (o)	0.000088 (o+inh)	-	?	0.00124 (o+inh)	No data on adults
PFOS, specific scenario	0.0068 (o)	-	-	?	0.0068 (o)	No data on adults
PFHxS, medium	0.00003 (o)	-	-	?	0.00003 (o)	No data
PFHxS, high	0.00005 (o)	-	-	?	0.00005 (o)	No data
Hydrocarbons						
Toluene, medium	-	9.1 µg/m^3 (inh)	-	-	9.1 µg/m^3 (inh)	No data
Toluene, high	-	55.3 µg/m^3 (inh)	-	-	55.3 µg/m^3 (inh)	No data
Toluene, specific scenario	-	230 µg/m^3 (inh)	-	-	230 µg/m^3 (inh)	No data
Xylenes, medium	-	7.5 µg/m^3 (inh)	-	-	7.5 µg/m^3 (inh)	No data
Xylenes, high	-	42.3 µg/m^3 (inh)	-	-	42.3 µg/m^3 (inh)	No data
Xylenes, specific scenario	-	146 µg/m^3 (inh)	-	-	146 µg/m^3 (inh)	No data
Ethylbenzene, medium	-	3.2 µg/m^3 (inh)	-	-	3.2 µg/m^3 (inh)	No data
Ethylbenzene, high	-	8.2 µg/m^3 (inh)	-	-	8.2 µg/m^3 (inh)	No data
Ethylbenzene, specific scenario	-	230 µg/m^3 (inh)	-	-	230 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, medium	-	79 µg/m^3 (inh)	-	-	79 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, high	-	232 µg/m^3 (inh)	-	-	232 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, specific scenario indoors	-	1500 µg/m^3 (inh)	-	-	1500 µg/m^3 (inh)	No data
C7-C12-hydrocarbontotal, worst-case use of the alkyd paint indoors	-	-	-	6 x 10^6 (inh)	6 x 10^6 (inh)	No data
Styrene, medium	-	-	-	-	-	No data
Styrene, high	0.18 (o)	2.5 µg/m^3 (inh)	-	-	0.18 (o)	No data

					2.5 µg/m^3 (inh)	
Metals						
Aluminium, medium	0.041 (int)	-		-	0.041 (int)	No data
Aluminium, high.	0.096 (int)	-		-	0.096 (int)	No data
Aluminium, specific scenario cosmetics			85.7 (int)		85.7 (int)	No data
Bly, medium	0.24 (o)	-	-	-	0.24 (o)	No data
Bly, high	0.84 (o)	-	-	-	0.84 (o)	No data
Mercury, inorg. medium	0.026 (o)	-	-	-	0.026 (o)	No data
Mercury, inorg. high	0.077 (o)	-	-	-	0.077 (o)	No data
Mercury, inorg. specific scenario (broken energy bulb)	0	-	-	0.28 (o)	0.28 (o)	No data
Methyl mercury, medium	0.018 (o)	-	-	-	0.018 (o)	No data
Methyl mercury, high	0.051 (o)	-	-	-	0.051 (o)	No data
Pesticides						
Diazinon, medium	0.0055 (o)	-	-	-	0.0055 (o)	No data
Diazinon, high	0.0086 (o)	-	-	-	0.0086 (o)	No data
Dimethoate, medium	0.0073 (o)	-	-	-	0.0073 (o)	No data
Dimethoate, high	0.012 (o)	-	-	-	0.012 (o)	No data
Chlorfenvinphos, medium	0.0033 (o)	-	-	-	0.33	No data
Chlorfenvinphos, high	0.0052 (o)	-	-	-	0.0052 (o)	No data
Methamidophos, medium	0.0034 (o)	-	-	-	0.0034(o)	No data
Methamidophos, high	0.0053 (o)	-	-	-	0.0053 (o)	No data
Oxydemeton-methyl (sum), medium	0.00086 (o)	-	-	-	0..0086 (o)	No data
Oxydemeton-methyl (sum), high	0.0014 (o)	-	-	-	0.0014 (o)	No data
Carbaryl, medium	0.05 (o)	-	-	-	0.05 (o)	No data
Carbaryl, high	0.079 (o)	-	-	-	0.079 (o)	No data
Carbendazim and benomyl, medium	0.10 (o)	-	-	-	0.10 (o)	No data

Carbendazim and benomyl, high	0.16 (o)	-	-	-	0.16 (o)	No data
Methomyl and thiodicarb, medium	0.010 (o)	-	-	-	0.010 (o)	No data
Methomyl and thiodicarb, high	0.015 (o)	-	-	-	0.015 (o)	No data
Phenols						
Bisphenol A, medium	0.132 (o. int)	0.084 (int) sum of indoor environment, cosmetics and articles			0.216 (o. nt)	0.03-0.04 µg/kg bw/d
Bisphenol A, high	0.388 (o. int)	0.678 (int) sum of indoor environment, cosmetics and articles			1.066 (o. int)	high: 0.13-0.24 µg/kg bw/d
Bisphenol A, specific scenario cash receipts		0.260 (int)			0.260 (int)	
Other substances						
Acrylamide, medium	0.5 (o)	-	-	-	0.5 (o)	No data on adults
Acrylamide, high	1.0 (o)	-	-	-	1.0 (o)	No data on adults

( ) : indicates that the dose is by oral ingestion (o), dermal exposure (d),inhalational exposure (inh), or the dose is calculated as internal dose (int)
- : no data, probably relatively poor
? : possible exposure of unknown size (on the existing basis data are missing, additional data will require more in-depth literature search and assessment)
Medium: indicates a typical exposure level, an average exposure or a median value
High: indicates a high but realistic exposure level, for example, expressed by a 95-percentile
Specific scenario: indicates a particular individual scenario typically with very high exposure

6.4 Observations in connection with the exposure tables

6.4.1 Food exposure

Tables 6.1 to 6.4 above show that in general exposure through food (incl. drinking water) is most well-described for the selected substances. This is primarily because many of the substances through many years have been known as substances of concern in food, and therefore have been subject to monitoring by scientists and authorities. This applies to a number of pesticides used in the treatment of food crops, and thus is subject to monitoring of contents of residues in foods. Other substances, for example bisphenol A and phthalates, are included in a number of polymer materials, which (more or less intentional) may occur in food contact material from which the substances by migration can be transferred into the food. Finally, it applies to a wide range of pollutants/ substances that are known to accumulate in the food chain, such as brominated flame retardants (HBCDD, TBBPA and PBDE compounds), the perfluorinated substances (PFOA, PFOS and PFHxS), PCB and dioxins, and heavy metals like lead and mercury.

6.4.2 Exposure via the environment

Particularly for small children of 1 to 3 years of age, the literature refers to exposure via the environment, because children in this age group through ingestion of dust from indoor air or play on the bare soil can achieve a significant exposure to chemical contaminants. This applies particularly to chemical substances contained in products used indoors as the substances when liberated from the products may occur in the indoor environment and its dust. For example, the contents of various flame-retardants in dust are due to the use of the substances in electronics or the use of flame-retardants in textiles or polymer materials for furniture and equipment. Content of PCBs in dust may be mainly due to evaporation or particles from sealing material containing PCBs, while the content of fluorinated compounds in the dust may derive from their use in textiles and other surface impregnation. Phthalate content in dust may originate from phthalate content in plastic products and fixtures, such as floors made of PVC plastic.

Finally, highly volatile substances such as hydrocarbons and tetrachloroethylene could occur in the indoor environment as vapours in connection with residues in consumer products and content in solvents in connection with application of paints and from cleaning fluid.

Furthermore, a lead is generally contained and measured in the dust in the indoor environment, and especially in larger cities soil will typically have elevated lead levels, which may contribute to lead exposure in small children when playing on and with the soil.

6.4.3 Cosmetics

Of the stated endocrine disruptors, suspected endocrine disrupters and neurotoxic substances, only relatively few substances can be identified, for which exposure through cosmetics can be considered significant.

This is the case for the UV-filters benzophenone 3 and 2-ethyl-4-methoxycinnamate (OMC), of which up to contents of 6% and 10 % are allowed in sunscreen as well as for D4 where exposure estimates for pregnant women/ unborn children also is based on use in sunscreen. In such cases a very significant exposure of users may occur. Exposure to the substances propyl paraben and butyl paraben may occur at a lower concentration, as the maximum permitted total content is 0.14 % in cosmetics, except for cosmetics intended for children up to 3 years where the use of the substances is not permitted in Denmark. However, exposure of children under 3 years is considered as well because parents may expose their children to cosmetics not specifically intended for small children. The medium exposure for children and pregnant

women/ unborn children covers use of cosmetics products (excluding sunscreen) containing these parabens, while high exposure, furthermore, covers the exposure from sunscreen. Exposure to Siloxan D4 is only estimated for pregnant women/ unborn children as no relevant data are available for children.

For women, exposure to aluminium via deodorant is estimated, while this type of exposure is not considered relevant for small children.

Finally, exposure to triclosan is estimated, because the substance still has a limited use in cosmetics, such as toothpaste (only found in toothpaste for adult, thus, no exposure to children).

For phthalates and bisphenols, it cannot be ruled out that there may be some exposure through cosmetics in the case of plastic packaging, from which the substances may migrate.

For the antioxidants BHT and BHA, the exposure estimates are based on the data obtained by analysis of cosmetic products in Chapter 5. The exposure assessments for children under 3 years and pregnant women/ unborn children are described in Section 6.6.1.

6.4.4 Exposure from other consumer products

For most substances, the data basis for population exposure through other consumer products can be considered as more sporadic than exposure from other sources, and exposure is highly dependent of actual content in a specific type of product of and how the products are used. Thus, some product may during specific periods be used in large amounts or to great extent and some product may be subject to mouthing by small children, or in otherwise have close contact to a person. Exposure to a number of substances from consumer products may also to some extent be reflected by the exposure from indoor environment, as the content in the indoor environment of the substances often will be a reflection of the use/ presence of consumer products containing the substances in the indoor environment.

For a number of substances, however, some data are available about content in consumer products/ articles and calculation of exposure. This applies, for example:

- Bisphenol (via cash receipts, adults)
- Phthalates (via various plastic objects, e.g. plastic sandals)
- Tetrachloroethylene (use of newly dry-cleaned clothes, adults)
- TCEP (e.g. baby sling with high content of flame-retardants, children)
- Hydrocarbons (use of paint (adults), evaporation from petrol can (children and adults))
- Lead (children sucking metal objects with residual content of lead, e.g. jewelry)
- Mercury (broken energy bulb (children)/ amalgam filling (adults))

For a number of the other substances, exposure via consumer products is considered minimal relative to the other sources, for example:

- Acrylamide
- PCB and dioxin
- Aluminium
- Mercury
- Pesticides

Finally, the extent of exposure directly from consumer products must be considered more uncertain for the substances:

- Brominated flame-retardants

- Bisphenol S and F
- Parabens
- PFOA, PFOS, PFHxS
- Certain phthalates
- D4
- Triclosan

as the secific use of these substances in consumer products is less well known, but can, however, not be ruled out.

6.5 Exposure assessment from biomonitoring data

In relation to biomonitoring data, focus has been on the studies with particular relevance for children under 3 years and unborn children in Denmark. Besides focusing on Danish studies, emphasis is on recent biomonitoring studies in countries similar to Denmark, where specific exposure estimates have been made from the measured biomonitoring data and where the studies are estimated to be comparable to Danish conditions. A complete list and assessment of the biomonitoring studies can be found in Appendix 6c.

The biomonitoring studies can contribute to the exposure estimation for the various substances, as measurements of the substances and/ or the metabolites in a biological sample, e.g. in blood or in urine, thereby reflecting the actual level of exposure of the person. When assessing the biomonitoring results, it is important to consider certain things.

Estimation of exposure based on biomonitoring data is mostly applicable for rapidly degradable substances measured in the urine, as these substances are often excreted or eliminated during the first 24 hours. Some substances are partly excreted through sweat or the exhaled air, which induces an uncertainty to the estimated exposure, as knowledge of thes degree of excretion through these routes are often not available for the individual substances. For persistent substances, the use of biomonitoring data to estimate exposure is more complicated, as the measured levels can be an indication of an exposure accumulated over time (sometimes years), and a balance between the levels in e.g. blood and fat or blood and binding to protein. Typically, the rapid degradable substances are measured in the urine, and in the majority of the selected studies, the measurements are carried out in morning spot urine.

To get a more accurate picture of the excretion of the substances, it may also be advantageous to use whole-day-urine instead of spot urine, as there might be fluctuations in the level of excretion of rapidly metabolised substances from morning to evening. Measurements made only on morning urine may therefore not always fully reflect the total excretion. Next, it is important to know the metabolism and kinetics of the substances in the body, so that any possible metabolites are included in the quantification, and so that exposure back-calculation can be made most accurately. In some cases, the metabolites of the substances are known, but it is not always the case, just as the exact percentage excreted in the urine is often highly uncertain. This is a significant source of errors in the estimation of the exposure based on biomonitoring data. In addition, there can be large variations among analytical methods and laboratories, which adds some uncertainty for the use of biomonitoring results for direct back-calculation and estimation of exposure.

As the biomarkers are typically measured in urine or blood, which may be more or less concentrated, it is important that the measured levels are normalised against a more stable factor. For urine samples, this is done typically by adjusting the measured concentration to the total creatinine excretion in the urine, as this is considered constant and independent of the amount of water in urine. The creatinine secretion depends on muscle mass and therefore varies be-

tween sex and age, and weight, and it is therefore important that the persons included in the biomonitoring studies are more or less homogeneous in terms of these parameters.

The summary table in Annex 6c briefly describes the selected biomonitoring studies for each substance. For most substances, the biomonitoring is performed in urine or blood samples. For some substances (e.g. PBDE substances, PCBs, parabens and some phthalates), measurements are made in breast milk from Swiss women, and finally there are mercury measurements made in hair. In addition, it can be seen in the table, whether specific exposure calculations from the measured biomonitoring data in the selected studies were made, and as far as possible, the estimates for the mean exposure and 95-percentile/ worst-case estimates are indicated.

Danish biomonitoring studies without exposure calculations are also included in the table in Appendix 6c, as it is considered relevant to supplement with all Danish knowledge in relation to assessing and/ or supporting the relevance of the estimation assessment of the substance/ substances.

The review of the studies in Annex 6c show estimation of the exposure levels, assessments based on urine measurements for acrylamide, bisphenol A, phthalates (DEHP, DBP, DiBP, BBzP, DINP), triclosan and the UV filter BP-3, respectively.
Especially for phthalates, highly relevant biomonitoring studies in both children and adults including exposure estimates based on the measured data have been identified. These, together with the modelled exposure estimates, will help to provide a picture of the exposure of the population groups.
For the remaining biomonitoring studies with urine data, it is generally seen that the detected concentrationss result in lower exposure estimates compared to the exposure estimates based on the calculated exposure from different sources.

Exposure estimates based on biomonitoring data are in Tables 6.1 to 6.4 indicated in the biomonitoring column to the right.

There may be several reasons for the differences between the modelled/ calculated data and estimates based on biomonitoring data. In general, the found biomonitoring data are not from studies with the purpose of examining the amount of exposure from the specific sources, but rather to provide a measurement for the total exposure for the surveyed substances at any given time, which not necessarily includes periods with the highest exposure. For example, biomonitoring data for BP-3 are not carried out to investigate the exposure to UV filters after use of sunscreen, but it is a part of a larger study conducted in autumn, where use of sunscreen will not be expected. Therefore, the measurements are rather an expression of background exposure and are therefore much lower than the modelled data with include estimates for use of sunscreen.

When calculating the exposure estimates based on urine data, information on the absorption, metabolism and excretion of the substances was considered and taken into account in the calculation. Most of the substances measured in the urine (such as parabens, phthalates and BP-3) are substances that are degraded and/ or excreted from the body within 24-48 hours. The measured urinary levels are therefore an expression of the exposure during the past 24 hours. As the exposure will typically vary from day to day, average measurements and the 5 – 95-percentiles can be used to describe the typical average exposure and the variation in the population.

The higher exposure levels obtained by modelled estimations (compared with exposure estimates from biomonitoring) may be a result of the use of rather conservative values for the various exposure parameters in the models, in order to avoid underestimation of the exposure

for the scenarios. Furthermore, the addition of many exposure scenarios at high level at the same time may also contribute to overestimating exposure compared to a more realistic exposure situation for a consumer.

Contrary to this, the estimation of infants' exposure from measurements of biomarkers in breast milk has led to high exposure estimates. This indicates that breastfeeding can be a significant source of exposure. Exposure estimation in these studies is based on the measured concentration of breast milk coupled with the ingested amount of breast milk for infants. This estimation can be compared with the alternative scenario without breastfeeding, where modelled exposure estimations are derived based on the chemical content in foods and other sources. As can be seen from Appendices 6a and 6c, biomonitoring based calculations for the perfluorinated compounds; tetra-BDE-47; penta-BDE-99 and for totalPCB (sum of 7 PCB congeners) provide a higher exposure through breast milk compared to the modelled exposure through foods. Although these studies were not based on breast milk from Danish mothers, and therefore may not be directly transferable to the Danish population, it indicates that infants who are breastfed may be exposed to relatively high exposures to certain substances that have accumulated in the mother.

In Appendix 6c, the exposure estimates from biomonitoring studies subsequently considered relevant for the risk assessment are indicated in **bold**. In the exposure tables above, these estimates are included in the biomonitoring column to the right.

6.6 Exposure assessments based on analyses in Chapter 5

6.6.1 Exposure to BHT and BHA from cosmetic products

Based on the measured content of BHT and BHA reported in Chapter 5, exposure scenarios can be set up for BHA and BHT regarding the use of cosmetic products.
It appears from Table 5.6 that BHT was found in 24 cosmetic products. The highest content of BHT of 0.32 % was found in sunscreen, while the second highest content of 0.23 % was found in body lotion. These are leave-on products used in relatively large quantities per time, and is also applied to large parts of the body. Use of these two products daily during a summer will be able to provide a realistic worst-case scenario for exposure to BHT.
According to Table 7.6, BHA is only found in one cosmetic product (body oil) and only at a very low concentration of 0.0039 %. Therefore, exposure to BHA through cosmetics will only contribute marginally compared to BHT and it seems less relevant to make a more detailed exposure assessment for this substance because the contribution would be insignificant compared to the contribution of BHT. Furthermore, the presence of the substance in cosmetics is considered rare according to the analyses.

Pregnant women/ unborn children:
Body lotion
According to the Scientific Committee SCCS (2016), a daily consumption of 7.82 g/d is used for risk assessment of body lotion. Therefore, with a content of BHT of 0.23 %, a woman of 60 kg will be exposed to:

Pregnant women,$_{exp.body\ lotion}$ (µg/ kg/ d) = (7.82 g/d x 10^6 µg/ g x 0.0023) / 60 kg = *300 µg BHT/ kg/ d*

Sunscreen
According to the Scientific Committee SCCS (2016), a daily consumption of 18 g/d is used for risk assessment of sunscreen. Therefore, with a content of BHT of 0.32 %, a woman of 60 kg will be exposed to:

Pregnant women,$_{exp.sunscreen}$ (µg/ kg/ d) = (18 g/d x 10^6 µg/ g x 0.0032) / 60 kg = *960 µg BHT/ kg/ d*

Overall exposure
For pregnant women, a total daily exposure of *1260 µg BHT/ kg/ d* can be calculated when both body lotion and sunscreen are used daily.

In a Cosmetic Ingredient Review (2002), the dermal absorption is indicated to a maximum of 4 %. This was estimated from an *in vivo* study in guinea pigs, in which excretion of radioactively labelled BHT and metabolites wss measured in urine after dermal exposure.
A total dermal exposure of 1260 µg BHT/ kg/ d corresponds to an internal dose not exceeding 50,4 µg BHT/ kg/ d from body lotion and sunscreen. From body lotion alone, the dermal exposure of *300 µg BHT/ kg/ d* corresponds to an internal dose not exceeding *12 µg BHT/ kg/ d*.

Children under 3 years:
According to the Scientific Committee SCCS (2016), the ratio between the skin surface area and the body weight is 1.6 times higher in children of 1 year compared to adults. This means that at the same exposure per cm^2, the exposure will be 1.6 times higher per kg body weight for children of 1 year compared to adults.

On this basis and with a child of 1 year as a representative of the group of children under 3 years, the following exposure can be calculated:

Children,$_{exp.body\ lotion}$ (µg/ kg/ d) = 1.6 x 300 µg/ kg/ d = *480 µg BHT/ kg/ d*
Children, $_{exp.sunscreen}$ (µg/ kg/ d) = 1.6 x 960 µg/ kg/ d = *1536 µg BHT/ kg / d*

Overall exposure
For children under 3 years, a total daily exposure of *2016 µg BHT/ kg/ d* can be calculated when both body lotion and sunscreen are used daily.

In a Cosmetic Ingredient Review (2002), the dermal absorption is indicated to a maximum of 4 %. This was estimated from an *in vivo* study in guinea pigs, in which excretion of radioactively labelled BHT and metabolites wss measured in urine after dermal exposure.

A total dermal exposure of 2016 µg BHT/ kg/ d corresponds to an internal dose not exceeding 81 µg BHT/ kg/ d.

6.6.2 Exposure to bisphenols and phthalates from pizza boxes

In connection with the analyses of pizza boxes, the migration study with 50 % ethanol as migration liquid caused separation of the individual cardboard layers of the box. Therefore, the analytical result can be regarded more as a total content of the substances in the packaging rather than an expression of the amount of substance migrating from the recycled layer in the middle of the cardboard to the surface.

On this background, the analysis made with Tenax absorbent material placed on the cardboard surface is considered more relevant to a typical exposure situation with migration from cardboard surface and into the pizza.
However, by analysis of the Tenax absorption material neither bisphenol A, bisphenol F nor phthalates were found in a measurable level (indicated by the detection limits of the individual substances see Table 5.6).

The detection limits of e.g. bisphenol A and DEHP were 10 µg/dm^2 and 5 µg/dm^2, respectively, corresponding to 1/4 and 1/6 of the amounts measured of these substances at the ethanol migration.

Although none of the substances were detected at the Tenax migration study, it is considered possible to make a worst-case exposure assessment using the detection limit from the Tenax study as a worst-case migration level the substances that were shown to be present in the cardboard in connection with ethanol migration.

From the Tables 5.4 and 5.5, the following worst-case migration is assumed:

Bisphenol A: 10 µg/dm^2
DEHP: 5 µg/dm^2
DBP: 5 µg/dm^2
DIBP: 5 µg/dm^2

For the substances DINP, BBP and DNOP, the findings at the ethanol migration were lower than the detection limit at the Tenax method, and therefore the content from the migration analysis with 50 % ethanol may be used in this case (although this migration method is considered to overestimate the migration significantly).

DINP: 36 µg/dm^2
BBP: 2.9 µg/dm^2
DNOP: 4.2 µg/dm^2

Based on these assumed migration values, the exposure when eating a pizza can be calculated.

Pregnant women:
Here it is assumed that a pregnant woman (60 kg) consumes 1 pizza with a diameter of 28 cm (the largest pizza boxes for a normal size pizza had a side length of 29 cm).

Pregnant women$_{exp.bisphenol\ A}$ = π x r^2 x 10 µg/dm^2 / 60 kg = 3.14 x 14cm^2 x 0.1 µg/cm^2 / 60 kg

Pregnant women$_{exp\ bisphenol\ A}$ = 1.0 µg/kg/d

Similarly, exposure to the phthalates can be calculated as:

Pregnant women$_{exp\ DEHP}$ = 0.5 µg/kg/d
Pregnant women$_{exp\ DBP}$ = 0.5 µg/kg/d
Pregnant women$_{exp\ DIBP}$ = 0.5 µg/kg/d
Pregnant women$_{exp\ DINP}$ = 3.6 µg/kg/d (at detection limit: 5 µg/kg/d)
Pregnant women$_{exp\ BBP}$ = 0.3 µg/kg/d (at detection limit: 0,5 µg/kg/d)
Pregnant women$_{exp\ DNOP}$ = 0.4 µg/kg/d (at detection limit: 0,5 µg/kg/d)

Children under 3 years
A child aged 1-3 (13 kg) is assumed to eat half a pizza.

For bisphenol A, the following exposure can be calculated:

Child$_{exp\ bisphenol\ A}$ = π x r^2 x 0.5 x 10 µg/dm^2 / 13 kg = 3.14 x 14cm^2 x 0.5 x 0.1 µg/cm^2 / 13 kg

Child$_{exp\ bisphenol\ A}$ = 2.4 µg/kg/d

Similarly, exposure to the phthalates can be calculated as:

Child$_{exp\ DEHP}$ = 1.2 µg/kg/d
Child$_{exp\ DBP}$ = 1.2 µg/kg/d
Child$_{exp\ DIBP}$ = 1.2 µg/kg/d
Child$_{exp\ DINP}$ = 8.6 µg/kg/d (at detection limit: 12 µg/kg/d)
Child$_{exp\ BBP}$ = 0.7 µg/kg/d (at detection limit: 1.2 µg/kg/d)
Child$_{exp\ DNoP}$ = 1.0 µg/kg/d (at detection limit: 1.2 µg/kg/d)

7. Hazard Assessment of the selected substances

7.1 Objective and method

The objective of the hazard assessment is to identify the critical effects and dose levels for endocrine disrupting and neurotoxic effects of the selected substances. These values will be used to establish tolerable exposure levels/ DNEL values (Derived No Effect Level).

For endocrine disrupting effects, the discussion is ongoing whether lower limits for effects can be established with reasonable certainty, or whether the alternative risk assessment method should be used instead of the traditional one. In this project, it is decided to use the traditional risk assessment method and establish DNEL values on this basis. If at some point, another method of risk assessment of endocrine disrupting effects is agreed, it may be necessary to reassess the values.

As the focus of the cumulative risk assessment in this project is endocrine disrupting or neurotoxic effects, it is chosen to use no-effect levels, NOAELs (No Observed Adverse Effect Levels), and lowest effect levels LOAEL'S (Lowest Observed Adverse Effect Levels) from data demonstrating endocrine disrupting or neurotoxic effects. These NOAELs/ LOAELs are not necessarily the most critical ones for the substance in question, as other harmful effects may result in lower N(L)OAEL values for some of the substances. However, it is intended specifically to select NOAELs/ LOAELs based on endocrine disruption or neurotoxic effects e.g. from data in EU risk assessments, EFSA opinions or other official risk assessments. In some cases, a benchmark dose approach is used. In such cases, a benchmark low dose (BMDL) for a 10 % effect size will be used as basis.

Already in the selection of the substances in Chapter 2 and in connection with the exposure assessment of substances, there has been a collection of comprehensive information in relation to the substances' effects and the establishment of tolerable human exposure levels. Where internationally accepted tolerable exposure levels have already been established, their application is discussed. In cases where additional information is collected, the relevance and validity of the available studies are evaluated. Where possible, the proposed mode of action behind the adverse effects is indicated, which can be used in the risk assessment where the risk contributions for substances with identical effects or mode of action are added.

Paracetamol is different from the other ingredients, as it is a medicinal product used for the purpose of the therapeutic/ beneficial effect, knowing that there may be side effects. Although, the risk assessment of medicinal products is basically different from risk assessment of chemicals from foods, cosmetics, indoor environment and other sources, we in this project have chosen to calculate a DNEL using the same principles for all substances in order to relate the calculated risk for endocrine disrupting effects for the various chemicals irrespective of the use of the chemical or the source of exposure.

For the selected endocrine disrupting and neurotoxic substances (or groups of substances), a brief description is made regarding the critical endocrine disrupting or neurotoxic effects, see Tables 7.1 and 7.2, respectively. Critical dose levels for the effects are identified based on experimental animal data and human data, and DNEL-values are calculated. The relevant data and the derivation of DNEL values are described in more detail in Appendix 7a (endocrine disruptors) and Appendix 7b (neurotoxic substances).

7.1.1 Method for hazard assessment of endocrine disrupting and suspected endocrine disrupting substances

In the assessment of the endocrine disrupting and suspected endocrine disrupting substances, focus in this report is on antiandrogenic, estrogenic or thyroid hormone disrupting mode of action. These modes of action can result in many different effects in animal studies, depending on species and the time in life, the animals are exposed to the substances.

For antiandrogenic mode of action, the effects observed in animal studies may be:

- changes in testosterone levels/ production,
- reduced sperm count, altered weight or histological changes in male reproductive organs, in combination with data indicating antiandrogenic effects in other studies (e.g. Hershberger assay or cell-based studies),
- reduced anogenital distance in males at birth,
- increased number of retained nipples (nipple retention) in young animals,
- malformed genitalia (hypospadias).

Some of these effects are considered harmful in themselves; while other effects are perceived as robust biomarkers for adverse effects (e.g. change in testosterone levels, decreased anogenital distance and retention of nipples). In such cases, a biomarker predicts that other harmful antiandrogenic effects of the substances will occur at higher levels of exposure, or in other types of studies than those available for the substance. Using a conservative approach, this report therefore uses all the above effects for establishing DNEL values.

Some effects observed in animal studies may be induced by substances with both antiandrogenic and estrogenic modes of action (e.g. delayed puberty, changes in testicular weight and sperm count). These effects appear in this report as antiandrogenic effect in cases where at the same time it is shown that the substance has other effects clearly attributable to antiandrogenic mode of action, maybe at higher doses or in other studies.

Studies are preferred where the effects are seen after exposure to the substance in the embryonic stage. For some substances, NOAEL/ LOAEL are selected based on studies on exposure of young or adult animals, given the lack of specific studies of antiandrogenic effects in animal studies with perinatal exposure. In these cases, there is also knowledge of antiandrogenic effects in other studies, e.g. screening test for antiandrogenic effect (Hershberger test) or cell based studies.

For estrogenic effect, NOAELs/ LOAELs are selected based on the different effects that may result from estrogenic mode of action in animal studies, i.e.

- early puberty or impaired female fertility,
- changes in the estrous cycle,
- increased uterine weight in uterotrophic assay,
- reduced sperm count, altered weight or histological changes in male or female reproductive organs (including breast tissue), if accompanied by knowledge of estrogenic effects in other studies (e.g. uterotrophic assay or cell-based studies).

Studies are used in which the effects are seen after exposure to the substance in the fetal stage, if these are found relevant. For several substances, however, NOAELs/ LOAELs are applied for the studies of animals dosed as adolescents or adults, including so-called screening studies (e.g. uterotrophic assay). This is considered relevant, as it has been shown that if estrogenic effects of exposure of adult animals are seen, there will also be estrogenic effects of exposure in the fetal stage, although the sensitivity may be different during the early development than later in life.

It is discussed whether changes in uterine weight in uterotrophic assay should be considered an adverse effect. In some studies, the animals have had their ovaries removed before being exposed to the substance and this is a very sensitive model for the influence of estrogenic substances that results in increased uterine weight. Uterotrophic assay can also be performed with intact immature animals, which are also sensitive to the influence of estrogen-like substances, but in those cases, it is a biologically relevant effect and there is less doubt that the effects on the uterine weight can be of concern. Effects on the uterus in uterotrophic assay are considered by many to be a sensitive marker for estrogenic mode of operation, as substances with effect in uterotrophic assay in many cases have other harmful effects in other types of studies. Using a conservative approach, this report therefore also uses effects on the uterus in uterotrophic assay for establishing DNEL values.

Some effects observed in animal studies may be induced by substances with both antiandrogenic and estrogenic modes of action (e.g. delayed puberty, changes in testicular weight and sperm count), but appear here as estrogenic effect, if further data indicate that the substance has other effects that are clearly attributable to estrogenic mode of action, maybe at higher doses or in other studies.

For thyroid hormone disrupting substances, NOAELs / LOAEL'S have been selected based on effects caused by a thyroid hormone disrupting effect in animal studies, i.e.

- reduction in T3 or T4 levels in the blood, possible increase of TSH,
- changed thyroid weight,
- histological changes (indicating hyperactivity) of the thyroid.

The effect, which in most studies is seen at the lowest dose, is reduction of the total T4 (thyroxine) levels in the blood, and therefore a significant decrease in T4 often forms the basis for selection of DNEL value. Substances that lower T4 in the blood can do this through a variety of thyroid hormone disrupting mechanisms, and it is for most of the substances shown that higher doses result in more serious thyroid hormone disrupting effects, in particular reduced T3 (triiodothyronine) levels, elevated TSH (thyroid stimulating hormone) levels, increased weights and histological changes of the thyroid. Although the reduction of T4 is not universally regarded as a harmful effect in itself, it is, however, chosen based on a conservative approach to use effects on T4 levels for establishing DNEL values in this project. When deriving the DNEL, studies are used where the effects are observed in pregnant and non-pregnant animals, as the effects on the thyroid hormones are assumed to occur at the same dose levels independent of whether the animal is pregnant or not.

Due to differences between the rat and the human thyroid system, it has for a long time been discussed whether T4 reductions in experimental animals are relevant for humans. Experts in this field have in recent years argued that especially when it comes to thyroid hormone disrupting potential on the developing nervous system, the measuring of T4 reductions in animals is quite relevant (Zoeller et al. 2007). Although significant physiological differences between the rat and the human thyroid system exist (such as the type of binding proteins in the blood; differences in thyroid storage capacity of thyroid hormones; faster decrease in T4 in a rat after exposure to a given endocrine disrupting substance than in humans), we do not know enough

from the animal models at the moment to determine if rats are more or less sensitive to the effects of decreased T4 (Crofton and Zoeller 2005; Zoeller et al. 2007). Since both species appear to be sensitive to lack of T4 during brain development, and some of the same mechanisms, therefore, seem to be relevant in rats as well as in humans (Crofton and Zoeller 2005; Crofton 2005), emphasis in this report is put on results showing reduced T4 levels by selection of LOAELs and NOAELs.

The significance of T4 reductions in humans is believed to be highest during the early development, i.e. in the embryonic stage, but this project calculates with the same DNEL for children and pregnant women regarding thyroid hormone disrupting effect. As pregnant women/ the unborn child thus are believed to be more sensitive than children regarding reduction of T4 levels, a risk assessment for children may overestimate the risk associated with exposure to thyroid hormone disrupting chemicals. However, it is not currently possible to determine whether - or how much - the risk may be overestimated.

7.1.2 Method for hazard assessment of neurotoxic substances

For chronic neurotoxic substances where a generally accepted tolerable exposure level (a TDI or DNEL established by EFSA or the ECHA risk assessment committee RAC or another international expert group/ organisation) have been provided, it will be examined whether the tolerable exposure level is derived considering the neurotoxic effects, or whether other critical effects have been the starting point for the derivation. If the critical effect for determining the tolerable exposure level is the neurotoxic effects, this TDI is used as DNEL value for this project.

If the starting point for calculating the tolerable exposure level has been other critical effects, data relating to the neurotoxic effects are examined closer to designate an appropriate N(L)OAEL level (No (Low) Observable Effect Level) that can form the basis for the establishment of a DNEL level specifically for the neurotoxic effects.

Fetuses and small children, whose nervous systems are under development, are particularly vulnerable to neurotoxic substances and their effects (Grandjean et al 2016). Therefore, it is evaluated for the selected substances, whether data describing the neurotoxic effects of the substances are related to the most sensitive periods of life. If this is not the case, it is assessed whether there is a need to apply an additional assessment factor to ensure the protection of children and unborn children. This approach is for example used in determining the DNEL values for selected organic solvents (hydrocarbons and tetrachloroethylene), where the data for neurotoxic effects are mainly related to the exposure of adult individuals.

Although the DNEL value for the neurotoxic effects can be determined from the high quality appropriate N(L)OAEL values (or BMDL values; BenchMark Dose Levels) from experimental animal data or human data, it is generally very difficult to identify specific mechanisms/ mode of actions behind the neurotoxic effects as can be done for many endocrine disruptors and their effects.

With regard to knowledge of mechanisms, mode of action for neurotoxic substances, Giordano and Costa (2012) indicate some possible (but not unequivocal) mechanisms of e.g. lead and methyl mercury's neurotoxic effects, while for other substances e.g. PBDEs the mode of action is described as unknown.

Similarly, knowledge is lacking regarding the mechanisms behind the neurotoxic effects of the organic solvents (e.g. hydrocarbon mixtures and tetrachloroethylene). However, for hydrocarbon mixtures, it is known that chronic neurotoxic effects develop after many years of exposure, and therefore short-term exceedance of the DNEL for hydrocarbons can be considered less serious compared with other neurotoxic substances, where short-term exposure in the development stage has caused lasting damage.

Within the area of pesticides, however, attempts have been made in recent years to group neurotoxic pesticide substances based on the knowledge of their mechanisms of action and their effects on the nervous system, in order to better assess the risk of concurrent exposure to the substances. In this context, numerous subgroups have been listed regarding the type of effects the substances may cause. A report from DTU Food Institute (Nielsen et al. 2012) proposed 17 different groups regarding either neurotoxic effects or neurotoxic mechanisms of pesticide substances. This indicates that it is very complex and difficult to make grouping of these substances. However, it can be noted from the report that the substances in the substance groups dithiocarbamates (cholinesterase inhibitors), organophosphates (cholinesterase inhibitors) and pyrethroids and pyrethrins as a result of their similar toxic effects and mechanisms of action can be assessed on a group basis.

In a report for EFSA, several organisations have continued working with data and recommendations specified by Nielsen et al. (2012) and found after thorough assessment of the data, that it was only possible to elucidate the mechanisms of action for very few pesticides (EFSA 2013). In this context, it was agreed that a group assessment of the neurotoxic effects of pesticide substances would be most justified for organophosphates and carbamates due to their similar mechanisms of action (cholinesterase inhibition). However, a specific method for this was not suggested in the report.

In an opinion regarding toxicology of mixed exposure from the three scientific committees in the EU (SCHER, SCCS, SCENIHR: Opinion on the Toxicity and Assessment of Chemical Mixtures, 2012) it is proposed that if the mechanisms behind the effects on a target organ are unknown, to apply a risk assessment method that uses the method of adding the hazard indices for the individual substances. In the context of REACH such hazard indices corresponds to the risk characterisation ratios. Thus, RCR values (Risk Characterisation Ratio) are added for the different substances that have effects on the same organ system.

Also, the advantage of this approach is that it takes into account that even if the substances do not have the same underlying mechanisms, they may, when they affect the nervous system, still have an overall combined influence on the nervous system. Thus, it may be assumed that different mechanisms can interact and promote adverse effects in the nervous system.

7.1.3 Use of assessment factors

REACH recommends derivation of DNEL values based on a NOAEL or an LOAEL and by the use of assessment factors (AF). Thus, a DNEL value may be calculated as follows (ECHA 2012):

$$\textit{Effect specific DNEL} = \textit{N(L)OAEL/ AF1 x AF2 x …AFn} = \textit{N(L)OAEL/ total AF}$$

The use of assessment factors depends on the type and quality of data on which the NOAEL or the LOAEL are based. If data is available, case-specific assessment factors should be used, but in the absence of data default values have been assigned for the assessment factors as given in Table 7.1.

Table 7.1 Assessment factors (AF) used for the calculation of DNEL

Parameter	Value	Used assessment factor
Interspecies	Allometric scaling factor i.e. correction for differences in metabolic rate per kg body weight.	4 for rats 7 for mice 2.4 for rabbit 2 for monkey
Interspecies	Remaining differences interspecies	2.5
Intraspecies	Differences in susceptibility between individuals	10
Dose-response	LOAEL to NOAEL, if LOAEL is used instead of a NOAEL	3-10

The use of assessment factors for derivation of DNEL for the neurotoxic substances in this project is shown in Table 7.3 and in Appendix 7b.

7.1.4 Hazard characterisation and DNEL for endocrine disruptors and suspected endocrine disruptors

Table 7.2 lists the critical effects and selected NOAEL/ LOAEL/ BMDL for the calculation of DNEL values for endocrine disruptors. A more detailed review and considerations regarding additional studies can be found in Appendix 6a. The experimental animal study underlying the DNEL determination is listed with indication of effect parameters, NOAEL, LOAEL or BMDL values. Absorption factors used for converting external to internal doses are indicated where possible, and if no knowledge is available regarding specific absorption fractions, 100 % absorption is assumed. For each substance an assessment is given of the robustness of data for the endocrine disrupting effect in experimental animals. It is generally assessed that the evidence is strengthened a) when there are several suitable animal studies showing adverse effects for reproduction and which are consistent with an endocrine mode of action, b) when there is no opposing evidence from the animal studies, and c) when suitable *in vitro* studies support the endocrine disrupting effect seen in animal studies.

For each substance, there may be more than one DNEL if the substance has several modes of action. DNELaa, DNELe and/ or DNELthyr are stated for substances with androgenic, estrogenic and/ or thyroid hormone disrupting mode of action, respectively. It should be noted that for bisphenol A, two DNEL values are determined for estrogenic mode of action, and details about the background of these two values are given in Appendix 6a. For PCBs, DNELaa and DNELthyr values are established for dioxin-like PCBs (assessed with dioxins) for the use in risk assessment of foods. See Appendix 6a for detailed description.

Table 7.2 Summary table for determining the DNELs for endocrine disruptors and suspected endocrine disruptors. References can be found in the reference list in Appendix 7a

Endocrine disruptors	Effect parameter and route of exposure (o=oral, sc=subcutaneous)	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELexternal (µg/kg bw/d)	DNELinternal (µg/kg bw/d)	References
			Antioxidants			
BHA	T: changes in T4, thyroid weight and histology, rat (o)	100/500/-	100	1000	1000	Jeong et al., 2005
BHT	T: changes in thyroid histology, rat (o)	25/108/-	100	250 (oral)	250	EFSA 2012b (Olsen et al., 1986; Søndergaard og Olsen, 1982)
			Brominated substances			
TBBPA	T: Decreased T4, rat (o)	30/100/16	(At least) 100 from BMDL10	160	160	EFSA 2011a (van der Ven et al., 2008)
HBCDD	T: changes in T4, thyroid weight and histology, rat (o)	-/-/22.9 (body burden -/-/0.38)	8 (EFSA 2011b)	48	41	EU RAR 2008, adjusted (van der Ven et al., 2006)
Deca-BDE	T: Decreased T3 and T4, rat (o)	-/6/6.8	2.5 from BMDL10 (EFSA 2011c)	2.7	2.7	EFSA 2011a
			Chlorinated substances			
Dioxins and dioxin-like PCBs	AA (foods and indoor environment): ↓ AGD in males, changed weight of male reproductive organs, ↓ serum testosterone			2E-06	2E-06	EC-SCF 2001 (Faqi et al., 1998)
Dioxins and dioxin-like PCBs	T (foods and indoor environment): Changed thyrod histology, decreased T4, increased TSH			6E-06	6E-06	(Sewall et al., 1995)
PCBs, total	AA (dust): Reproductive effects	-/0.0005/-	2,5*2*10*3=150	3.3E-03	3.3E-03	(Arnold et al., 1995)

Endocrine disruptors	Effect parameter and route of exposure (o=oral, sc=subcutaneous)	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELexternal (µg/kg bw/d)	DNELinternal (µg/kg bw/d)	References
			Fluorinated substances			
PFOA	T: Decreased T4, increased TSH, monkey 26 weeks (o)	NA/3/-	2.5*2*10*3=150	20	20	(Butenhoff et al., 2002)
PFOS	AA: Decreased testosterone and decreased expression of genes related to steroid synthesis, rat (o)	-/5/- human equivalent dose HED: -/0.007/-	3*2.5*4*10=300 from HED: 3*3*10=90	17	17 from HED: 0.08	(Zhao et al., 2014)
PFOS	T: Decreased T3 and T4, increased TSH, monkey (o)	0.0031/0.013/- (human equivalent dose)	30	-	0.1	US EPA 2016 (Seacat et al.,2002)
PFHxS	T: Decreased T3 and T4, rat (o)	0.05/5/-	300 from LOAEL	17	17 (not adjusted to human equivalent dose)	Ramhøj et al., 2015
			Phthalates			
DEHP	AA: ↓ AGD, ↑ Nipples, histological changes in testicles , male rat (o)	5/10/-	2.5*4*10 = 100	50 (oral)	35 (oral absorption of 70%; ECHA/RAC 2012)	EU RAR 2008 and ECHA/RAC 2012 (Wolfe and Layton 2003; Christiansen et al. 2010)
DEHP	T: Changed thyroid histology, rat (o)	37.6/375.2/-	2,5*4*10 = 100	376	263 (oral absorption of 70%; ECHA/RAC 2012)	(Poon et al. 1997)
DBP	AA: Changes in breast tissue, histological changes in testicles rat	Not established/2/-	2.5*4*10*3 = 300	6.7	6.7	EFSA 2005a, ECHA/RAC 2012 (Lee et al.,2004)
DiBP	AA: read-across from DBP	-/2.3/-	2.5*4*10*3 = 300	8.3	8.3	ECHA/RAC 2012 (Saillenfait et al.,2008)
BBP	AA: ↓ AGD, male rat	50/250/-	2.5*4*10 = 100	500	500	EFSA 2005b, ECHA/RAC 2012 (Tyl et al., 2004)
DPP	AA: ↓ AGD PND2, ↓ expression of steroid	33/100/-	2.5*4*10 = 100	330	330	(Hannas et al.,2011B)

Endocrine disruptors	Effect parameter and route of exposure (o=oral, sc=subcutaneous)	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELexternal (µg/kg bw/d)	DNELinternal (µg/kg bw/d)	References
	genes in fetal testicles, male rat					
DnHP	AA: ↓ AGD, increased frequency of malformations, male rat	50/125/-	2.5*4*10 = 100	500	500	(Saillenfait et al.,2009b)
DnHP	T: Thyroid histological effects, hyperactivity, rat	Not established/1824/-	2.5*4*10*3 = 300	6100	6100	(Hinton et al.,1986)
DnOP	T: Thyroid histological effects in a 13-week study, rat	36.8/350/-	2.5*4*10 = 100	368	368	(Poon et al.,1997)
DiNP	AA: ↑ Nipples, male rat (o)	300/600/-	2.5*4*10 = 100	3000	1500 (50 % oral absorption; ECHA 2013)	Boberg et al. 2011
DPHP	T: Thyroid histological effects in a 13-week study, rat (o)	-/-/10	100	100	100	Bhat et al., 2014, with reference to study by BASF AG (2009)
DCHP	AA: Changes in reproductive organs, ↓ AGD, ↑ Nipples, male rat	18/90/-	100	180	180	Hoshino et al., 2005
DCHP	T: Thyroid histological effects and increased weight	90/457/-	100	900	900	Hoshino et al., 2005
		Medicine				
Paracetamol	AA: ↓ AGD, rat	-/150/-	300	500	500	Holm et al., 2016; Kristensen et al., 2011
		Parabenes				
Butyl- and propyl paraben	E: Decreased sperm quality, rat (o, sc, respectively)	2/10/-	2.5*4*10=100	20	20	SCCS 2013 (Fisher et al., 1999, subcutan)
		Phenols				
Bisphenol A (1)	E: Reproductive effects and breast development in offspring, rat (o)	-/-/0.1 (human equivalent dose	25 (from HED)	4 (for comparison with external hu-	NA	EFSA 2015 (Delclos et al., 2014)

Endocrine disruptors	Effect parameter and route of exposure (o=oral, sc=subcutaneous)	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELexternal (µg/kg bw/d)	DNELinternal (µg/kg bw/d)	References
		adjusted for uncertainties in database)		man oral dose)		
Bisphenol A (2)	E: Breast development in offspring, rat (o)	0.025/0.080/- (rat) 0.018/0.057.6/- (human equivalent dose HED)	25 (from HED)	0.7 (for comparison with external human oral dose)	NA	DTU 2015 (Delclos et al., 2014)
Bisphenol F	E: increased uterine weight, young rat (sc)	50/100/-	100	500	500	Stroheker et al., 2003
Bisphenol S	E: increased uterine weight, young rat (sc)				500	Stroheker et al., 2003 (study of Bisphenol F)
Nonylphenol	E: Changes in reproductive organs, female and male, decreased sperm quality, rat (o)	15/50/-	2.5*4*10=100	150	15 (oral absorption factor of 10 %, EU RAR)	EU RAR 2002, NTP 1997,
			Pesticides			
Linuron	AA: Changes in male reproductive organs, increased retention of nipples in males at high dose, rat	12.5/25/-	100	125	125	McIntyre et al. 2000
Diazinon	E: Decreased sperm quality, estrogenic activity in cell studies	7/35/-	100	70	70	EFSA peer review
Dithiocarbamates (mancozeb, maneb, probineb)	T: Decreased T3 and T4, increased TSH and thyroid weight, changed thyroid histology, rat (o)	4.8 (125 ppm) / 28 (750 ppm) / -	2.5*4*10=100	48	48	(Stadler et al., 1990)
Pirimiphos-methyl	AA/E: Decreased sperm count, histological changes in the testes, rat. Androgenic and estrogenic activity in cell studies.	62.5/125/-	2.5*4*10=100	625	625	(Ngoula et al., 2007)
Procymidon	AA: ↓ AGD, hypospadias, testicular effect, rat	Not established/2.5/-	2.5*4*10*3*3=900	2.8	2.8	(EFSA 2009)
			UV-filters			
BP-3	E: Increased uterus weight in uterus test on immature rats	937/1525/-	2.5*4*10=100	9370	9370	(Schlumpf et al., 2001)

Endocrine disruptors	Effect parameter and route of exposure (o=oral, sc=subcutaneous)	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELexternal (µg/kg bw/d)	DNELinternal (µg/kg bw/d)	References
OMC	T: Decreased T4, rat	100/333/-	2.5*4*10=100	1000	1000	(Klammer et al., 2007)
OMC	E: Decreased sperm count and effects on reproductive organs in males (estrogenic mode of action in screening studies)	-/500/-	2.5*4*10*3=300	1667	1667	(Axelstad et al., 2011)
		Other substances				
Triclosan	E: Decreased weight of reproductive organs, changes in hormone levels, decreased sperm count, adult male rats	75/150/-	2.5*4*10=100	750	750	Stoker et al 2010
Triclosan	T: Decreased T4 after 31 days dosing of young male rats	3/30/-	2.5*4*10=100	30	30	(Zorilla et al., 2009)
Siloxane D4	E: Decreased fertility and decreased litter size, rats (inhalation), supported by increased uterine weight in uterus tests on rats and mice	19,5/32,5/-	2.5*4*10=100	195	195	(Siddiqui et al., 2007)

7.1.5 Hazard characterisation and DNEL for neurotoxic substances

Table 7.3 lists the critical effects and selected NOAEL/ LOAEL/ BMDL for calculation of DNEL for the neurotoxic substances. A more detailed presentation is provided in Appendix 7b.

Table 7.3 Summary table for determination of DNEL values for chronic neurotoxic effects

Neurotoxic substances	Effect parameter (and route of exposure; o, d, inh, int))	NOAEL/ LOAEL/ BMDL (mg/kg/day)	Assessment factors	DNELexternal (µg/kg/d)	DNELinternal (µg/kg/d)	References
Acrylamide	Degeneration of the sciatic nerve (o)	-/-/ 0.43 as $BMDL_{10}$ -value	12.5x10= 125	3.4 (o)	-	EFSA 2015
Aluminium	Reduced grip strength (o)	30/100/-	10x10=100	300 (o)	0.3	SCCS 2014. JECFA 2012
Bisphenol A	Adverse effects on brain and behaviour (o)	0.05/0.5/-	10x10x3 = 300	0.16 (o)	0.005	ECHA/RAC 2015
Lead	IQ loss in children (int)	-/-/0.0005* as $BMDL_{01}$-value	10	DMEL = 0,05 (o)	-	ECHA/RAC 2014
Deca-BDE	Changes in behaviour (o)	-/-/1.70* $BMDL_{10}$	2.5	680 (o)	-	EFSA 2011b
BDE-47	Changes in behaviour (o)	-/-/172 ng/kg/d* $BMDL_{10}$	2.5	0.07 (o)	-	EFSA 2011b
BDE-99	Changes in behaviour (o)	-/-/4.2 ng/kg/d* $BMDL_{10}$	2.5	0.0017 (o)	-	EFSA 2011b
BDE-153	Changes in behaviour (o)	-/-/9.6 ng/kg/d* $BMDL_{10}$	2.5	0.0038 (o)	-	EFSA 2011b
HBCDD	Changes in behaviour (o)	-/-/0.003* $BMDL_{10}$	2.5x3.2=8	0.4 (o)	-	EFSA 2011b
Hydrocarbons **hexane** **toluene** **xylenes** **ethylbenzene** **styrene** **methylstyrene** **propylbenzene** **trimethylbenzenes** **diisopropylbenzene** **phenyloctan** **C7-C12 hydrocarbons**	Chronic neurotoxic effects	Regarding identification of NOEL/ LOAEL, the use of assessment factors, and special attention to children's exposure and sensitivity, see the description in Danish EPA (2016)		**mg/m³** 0.700 (inh) 0.725 (inh) 0.125 (inh) 0.200 (inh) 0.175 (inh) 0.200 (inh) 0.240 (inh) 0.100 (inh) 0.200 (inh) 0.275 (inh)	- - - - -	Danish EPA 2016

total				1.425 (inh)		
Mercury, inorganic	Hearing loss, behaviour (o)	-/0.37/-	17.5x10x3 = 525	0.70 (o)	-	EFSA 2012
Mercury as methylmercury	Decreased performance in neuropsychological tests, learning	0.0012*/-/-	2 x 3.2 = 6.4	0.19 (o)	-	EFSA 2012
PCB, total	Changes in behaviour (o)	-/0.0075/-	5x10x3=150	0.05 (o)	-	Danish EPA 2014
PCB, dioxin-like + dioxins	Changes in behaviour (o)	-/20 pg/kg/d TCDD eqv.*/-	3.2x3= 10	2 pg/kg/d (o) TCDD eqv.	-	SCF 2001
PFOA	Assessed as PFOS	as PFOS	as PFOS	0.03 (o)	-	US EPA 2016a+b
PFOS	Changes in behaviour (o)	0.00084*/0.0025*/-	3x10=30	0.03 (o)	-	US EPA 2016b
TCEP	Damage to brain tissue (o)	31.5/63/-	10x10=100	315 (o)	-	EU RAR 2009
Tetrachlorethylen	Effect on colour vision (inh)	33/-/-	5x4=20	1.65 (inh)	-	Danish EPA 2016
Pesticides						
Organophosphates	Both organophosphates and carbamates exert their pesticidal effect by means of the substances inhibiting the enzyme acetylcholinesterase in the nervous system.					Jensen et al. 2015
Diazinon				0.2 (o)		The ADI values established at EU level and as specified by Jensen et al. (2015) are considered relevant as DNEL values for the protection for neurotoxic effects as well.
Dimethoate				1.0 (o)		
Chlorfenvinphos				0.5 (o)		
Methamidophos				1.0 (o)		
Oxydementon-methyl				0.3 (o)		
Carbamates						
Carbaryl				7.5 (o)		
Benomyl				20 (o)		
Methomyl				2.5 (o)		

* via toxicokinetic modelling converted into human dose prior to application of assessment factors.

It was not possible to determine a DNEL value for *PFHxS due* to lack of data and therefore no quantitative risk assessment for this substance can be made in the project.

7.2 Use of the DNEL values

In the next chapter, the derived DNEL values will be compared in a risk assessment context with the exposure values for the substances listed in Chapter 6. It should be noted that both exposure values and DNEL values for the substances may be associated to a specific exposure route or specified as internal exposure. Thus, there may subsequently in some cases still be a need for adjustment of the exposure values in relation to the exposure route in order to achieve a relevant comparison between exposure and DNEL value.

8. Risk assessment

8.1 Method

In this chapter, risk assessments of the selected substances are carried out. The risk assessments are carried out based on the exposure scenarios and the exposure estimates for children under 3 years and pregnant women/ unborn children as specified in Chapter 6 in relation to the tolerable exposure levels (DNEL values), which have been derived for endocrine disrupting and chronic neurotoxic effects, respectively, in Chapter 7.

As described in Chapter 6, scenarios with "medium" exposure represents a typical exposure using average values or median values. Scenarios with "high" exposure are usually an expression of realistic worst-case or 95-percentile exposures. In the cases where data are used for individual scenarios (typically specific worst-case scenarios), this is described in "special scenarios".

For risk assessment, the risk characterisation ratio is calculated:

$$RCR = exposure\ (\mu g/kg/d) / DNEL\ (\mu g/kg/d)$$

or by inhalation:

$$RCR = exposure\ (\mu g/m^3) / DNEL\ (\mu g/m^3)$$

The DNEL values in Chapter 7 are as far as possible based on already established tolerable exposure levels determined by expert committees, provided that the value is calculated precisely from the effects that are relevant for this project (i.e. endocrine effects (antiandrogenic, estrogenic or thyroid hormone disrupting effects) and chronic neurotoxic effects). In the cases where *no* tolerable exposure levels have been established by expert groups in relation to the effects mentioned above (i.e. other critical effects have been used for their DNEL derivation), a specific DNEL value relevant for the effects considered in this project has been calculated in Chapter 7. This means that a DNEL value for endocrine disrupting or chronic neurotoxic effects may be different from a tolerable exposure level established by a group of experts.

In cases where there are several relevant exposure routes, e.g. both oral and dermal exposure, the total RCR for contribution from both exposure routes is calculated by calculating the total dose absorbed in the body (internal dose), using knowledge of the absorption fraction for the dermal and the oral exposure routes, before the calculated internal dose contributions are added. Similarly, the DNEL value may be adjusted with the relevant absorption factor with respect to the route of exposure that forms the basis of the DNEL value.

RCR values above 1 indicate that the exposure is above the DNEL level, and that there is a potential risk depending on the size of the value.

Paracetamol is different from the other ingredients, as it is a medicinal product and is used for the purpose of the beneficial effect, knowing that there may be side effects. Therefore, the risk assessment of a medicinal product is basically different from risk assessment of chemicals from foods, cosmetics, indoor environment and other sources. In this project we chose, however, to calculate a DNEL using the same principles for all substances in order to relate the

calculated risk for endocrine disrupting effects for the various chemicals irrespective of the use of the chemical or the source of exposure. This is discussed further in section 8.2.9.

For values below 1, the exposure is lower than the DNEL level and the exposure is not considered to cause concern in relation to a potential risk for adverse effects.

It should be emphasised that an RCR value should always be assessed in relation to the uncertainties that are associated both to the exposure estimation as well as to the derivation of the DNEL value. Here, it is especially important for values close to 1 to discuss these uncertainties in more detail. Thus, it may be relevant to subsequently collect more data with regard to exposure parameters to update and refine the exposure assessment or possibly analyse the toxicological studies more closely (including incorporating any new studies) to assess whether the DNEL value should be adjusted in order to make the overall risk assessment more precise.

The RCR values are calculated for each substance and for each effect type (antiandrogenic, estrogenic or thyroid hormone disrupting effects as well as chronic neurotoxic effects).

An RCR value for a single substance is an indication of a potential risk related to the exposure from this single substance and thus does not take into account the interacting effects of simultaneous exposure to other substances. The effect of exposure to various substances with the same mode of action (or the same effect), can be described as the combined effect. The meaning of “mode of action” here is the way substances influence physiological processes, whereas the meaning of “effects” is the result (the damage) of this influence. It is known that exposure to several substances with similar effects often leads to increased toxicity in accordance with the principles of dose-additivity, and in Chapter 7, it is reasoned that this project will make an overall risk assessment for substances with the similar modes of action/ effects by adding the RCR contributions from these substances.

The overall risk can be expressed as the sum of the RCR values for substances with the same mode of action or with adverse effects at the same target organ:

$$RCR(total) = RCR(substance1) + RCR(substance2) + RCR(substance3) \ldots$$

Such RCR (total) values should be evaluated assessed with great caution, as the uncertainties of the individual RCR values are also added with this approach.

8.2 Risk assessment for endocrine disrupting effects

It is currently under discussion whether a lower limit for the effects of endocrine disruptors can be established (i.e. whether there is a threshold level for effects), and thus whether robust tolerable exposure levels can be derived. As an alternative method to assess the exposure risk of endocrine disrupting substances has not been established yet, a traditional risk assessment using the threshold approach is used here. An advantage of this approach is that the risk of the combined exposure to multiple substances with the same modes of action can be calculated. If in future an agreement can be reached regarding an alternative way to risk assess the endocrine disruptors, the calculations in this report should of course be reviewed. Such an alternative assessment method is considered to result in lower acceptable exposure levels and thus a higher estimated risk.

Here, the RCR value is called RCRaa for substances with antiandrogenic effects, RCRe for substances with estrogenic effects and RCRthyr for substances with thyroid hormone disrupting effects. For the substances with established DNEL values for several modes of action, several RCR values are calculated.

For each of the three effect groups a total RCRtotal is calculated: RCRtotal _aa for antiandrogenic substances, RCRtotal_e for the estrogenic substances and RCRtotal_thyr for the thyroid hormone disrupting substances. The endocrine disrupting substances are divided based on modes of action, but some antiandrogenic and some estrogenic substances may result in the same types of effects, despite the fact that they are believed to have different modes of action. Therefore, RCRtotal_aa + e are also calculated for the group of substances that affects the sex hormone balance.
As exposure data are calculated for scenarios with medium and high exposure, respectively, RCRtotal values are calculated for each of the three effect types for both scenarios.

The scenario with medium exposures thus shows the risk associated with total exposure to groups of chemicals for the average population. However, it should be noted that the exposure calculation for the medium scenario also includes e.g. the use of UV filters in sunscreen, which is only relevant part of the year. The scenario with high exposure indicates the risk associated with total exposure to high levels of these groups of chemicals simultaneously. It should be noted that it is less likely that humans are exposed to very high levels of all these chemicals at the same time, so RCRtotal for the scenario with high exposures represents a calculated risk to a minor part of the population. The proportion of the population exposed to high levels of the several of the substances at the same time is not known.

8.2.1 Cumulative risk assessment for endocrine disruptors (RCR_{total} for medium and high exposure)

Figure 8.1 shows the overall RCRtotal values for groups of substances with AA, E and T modes of action, respectively. An overall assessment of the sum of RCRs at medium exposures for children shows that RCRtotal > 1 for both the AA, E and T-groups, but for the unborn children, RCRtotal is just below 1 for all groups. This indicates a potential risk endocrine disrupting effects for the medium scenarios for children. For unborn children the RCRtotal values and thus the potential risk are lower – however, consideration should be paid to huge uncertainties as discussed below.

For scenarios with high exposure, the sum of RCRs is well over 1 for all effect groups, indicating that the risk of endocrine disrupting effects is not controlled for the part of the population with high simultaneous exposure to these chemicals.

Note that RCR for paracetamol is not included in the following figures and descriptions of data as very high RCR values are seen for Paracetamol, both for children and adults, and in both scenarios for medium and high exposure, i.e. by intake of 25 % and 100 %, respectively, of the maximum recommended daily dose. As the intake of paracetamol as a medicinal product can be controlled by the consumers, the substance is left out of the graphic illustration. It should be noted that Paracetamol is different from the other substances, as it is a medicinal product and is used for the purpose of the beneficial effect, knowing that there may be side effects. Therefore, the risk assessment of medicinal products is basically different from risk assessment of chemicals from foods, cosmetics, indoor environment and other sources. In this project we chose, however, to calculate a DNEL using the same principles for all substances in order to relate the calculated risk for endocrine disrupting effects for the various chemicals irrespective of the use of the chemical or the source of exposure. See also the discussion regarding risk assessment of paracetamol in Section 8.2.9.

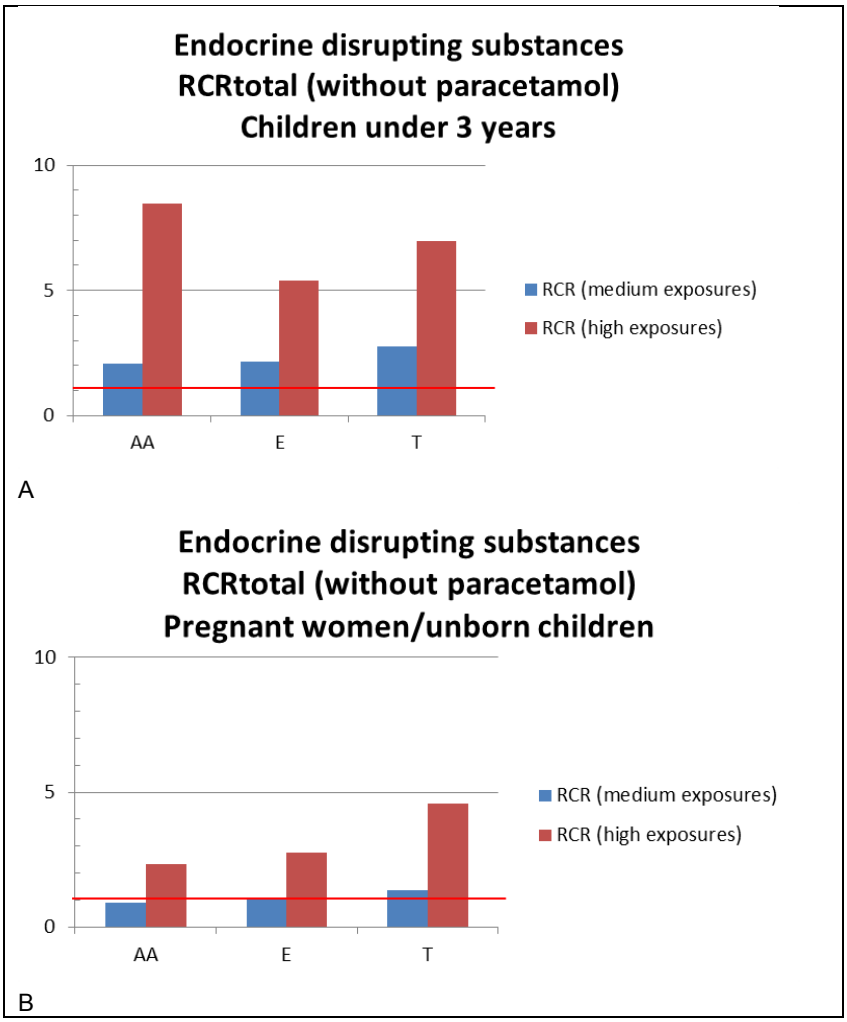
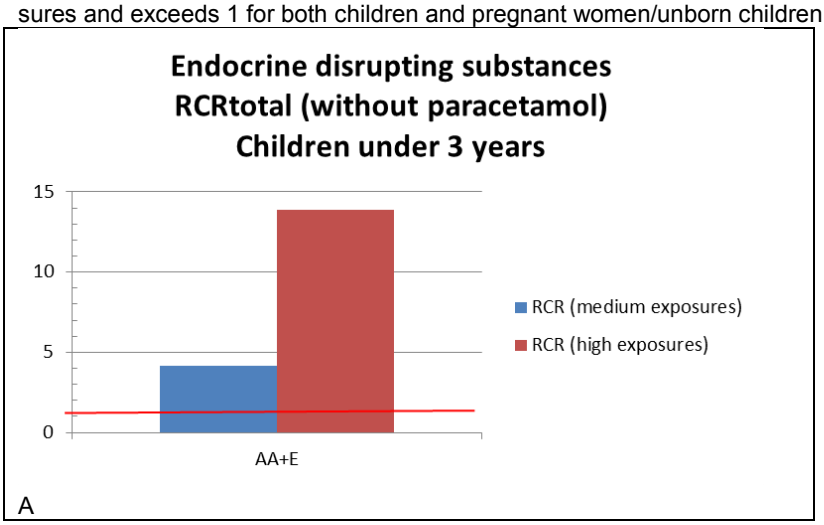


Figure 8.1. RCR_{total} for scenarios with medium and high exposure. A: children, B: pregnant women/ unborn children. Red line marks RCR=1. RCR values >1 indicates a potential risk from exposure to this group of substances.

An overall RCRtotal(aa + e) is calculated for antiandrogenic and estrogenic substances as several of the substances have the same types of effects in animal studies, and as it is shown that grouping based on knowledge of common effects can be just as relevant as grouping based on common modes of action (Nielsen 2011, EFSA 2013). Figure 8.2 shows that this overall grouping leads to an increased RCRtotal both for medium scenarios and for high exposures and exceeds 1 for both children and pregnant women/unborn children.



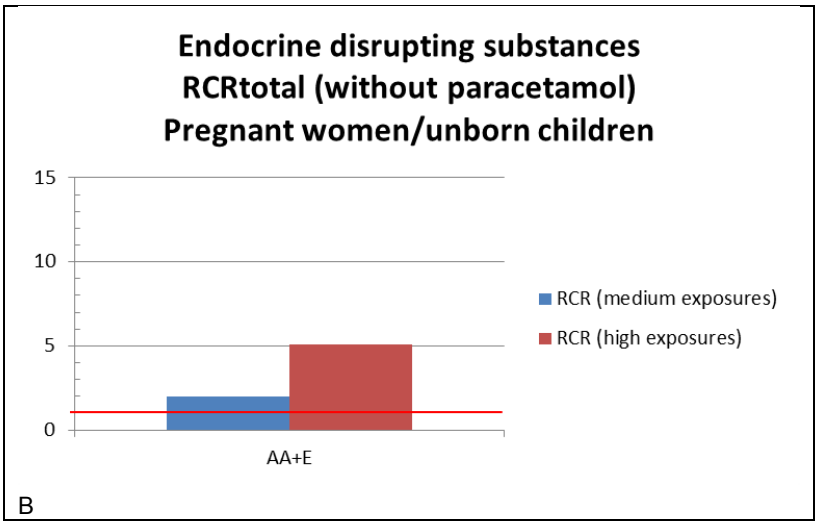


Figure 8.2 RCR_{total} added for antiandrogenic and estrogenic substances. A: children, B: pregnant women/ unborn children. Red line marks RCR=1. RCR values >1 indicates a potential risk from exposure to this group of substances.

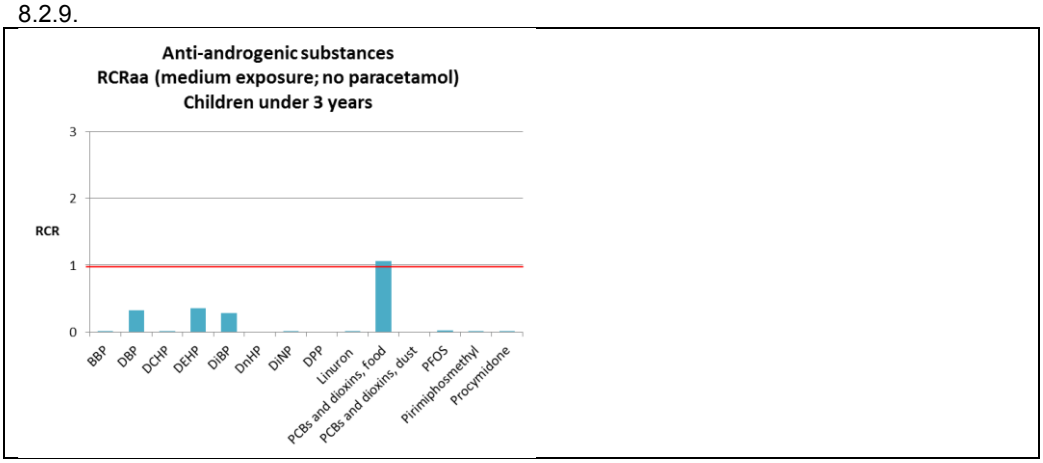
The individual substances that contribute to RCRtotal for each group of substances are listed in the following bar charts where the height of the bars partly reflects the individual substances' RCR value and partly gives a sense of how much the individual substance relatively contributes to the overall RCRtotal.

8.2.2 Antiandrogenic substances

Figure 8.1 shows that RCRaa total exceeds 1 for children (RCR above 8) and pregnant women/ unborn children (RCR above 2) in the scenario with high exposures, but just above and just above 2 for children and just below 1 for pregnant women/ unborn children in the scenario with medium exposures.

Children under 3 years – medium and high exposure

Paracetamol contributes with by far the highest RCRaa values. In scenarios for medium and high exposure, i.e. by daily intake of 25 % and 100 %, respectively, of the maximum recommended daily dose, RCRaa values are 25 and 100, respectively, for children (see Appendix 8 and Table 8.6). Figure 8.3 shows that in the scenario with medium exposures, a significant contribution is seen from dioxins and PCBs in foods (RCRaa = 1), while also three phthalates (DBP, DEHP and DIBP) constitute a major contribution (RCRaa about 0.3 for each phthalate). In the scenario with high exposures, the same substances contribute, but particularly the dioxin-like PCBs in the indoor environment (dust) contribute significantly to the overall RCRtotal_aa for children. See discussion regarding sources of exposure in the discussion Section 8.2.9.



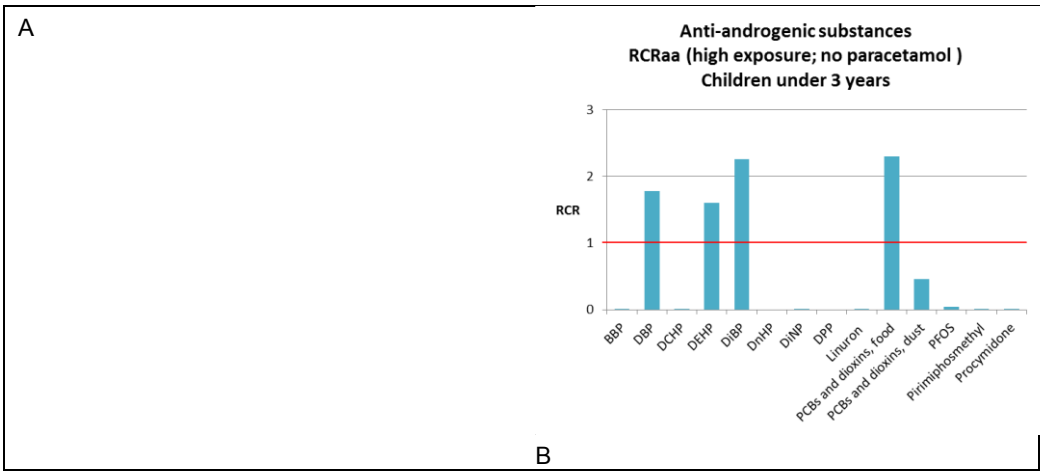


Figure 8.3. RCR values for children's exposure to individual substances with antiandrogenic effects. A: RCR values based on medium exposure; B: RCR values based on high exposure.

Pregnant women/ unborn children – medium and high exposure

Paracetamol contributes with by far the highest RCRaa values. In scenarios for medium and high exposure, i.e. by daily intake of 25 % and 100 %, respectively, of the maximum recommended daily dose, RCRaa values are 33 and 133, respectively, for pregnant women/ unborn children (Appendix 8 and Table 8.6). For pregnant women/ unborn children, minor contributions to RCRaa are seen from three phthalates in both scenarios, and in the scenario with high exposures, a substantial contribution is seen from dioxin-like PCBs in food. No RCR values for PCBs in dust could be calculated for pregnant women/unborn children, see Section 8.2.9.

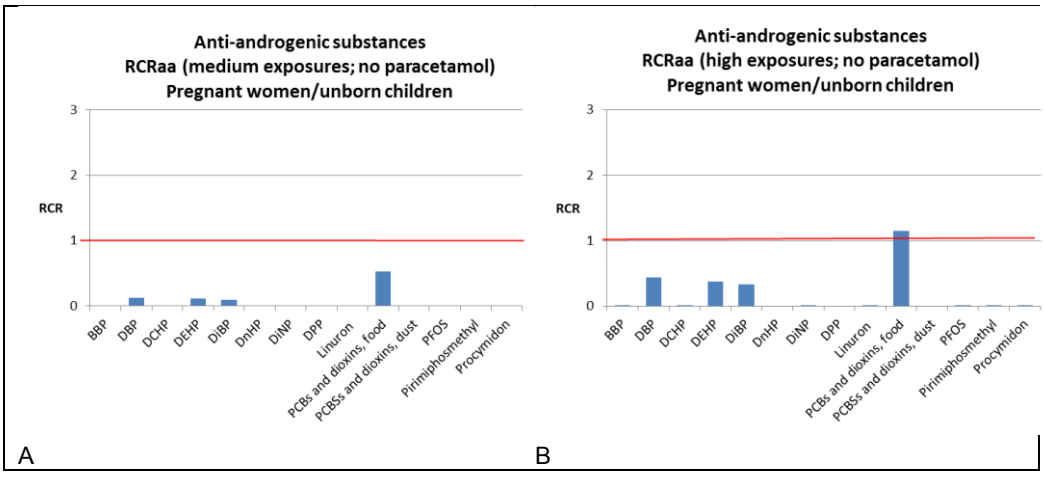


Figure 8.4. RCR values for exposure of pregnant women/ unborn children to individual substances with antiandrogenic effects. The sum of the shown RCRaa values is stated above each figure. A: RCR values based on medium exposure; B: RCR values based high exposure.

8.2.3 Estrogenic substances

It appears from Figure 8.1 above that RCRtotal for estrogenic substances is higher than 1 for both medium and high exposures of children and pregnant women/ unborn children. However, the RCRtotal value is only just above 1 in the scenario with medium exposures for pregnant women/ unborn children.

Children under 3 years – medium and high exposure

Figure 8.5 shows that for medium exposure, no individual substance has RCRe> 1, but in the scenario with high exposure butyl - and propyl paraben have RCRe> 1. In addition to the two

parabens (RCRe = 0.95), the UV filters BP-3 and OMC contribute with RCRe values of 0.2 for children in the scenario with medium exposures. It should be noted that this scenario includes use of sunscreen of 9 g per day for OMC and BP-3. The scenario with high exposure includes the use of 18 grams of sunscreen per day for OMC and BP-3, and 36 g of sunscreen per day for butyl- and propyl paraben (Appendix 6a). See detailed discussion of the sources of the individual substances below (Section 8.2.9). The scenario with high exposure also has contributions from bisphenol A and nonylphenol to the total RCR.

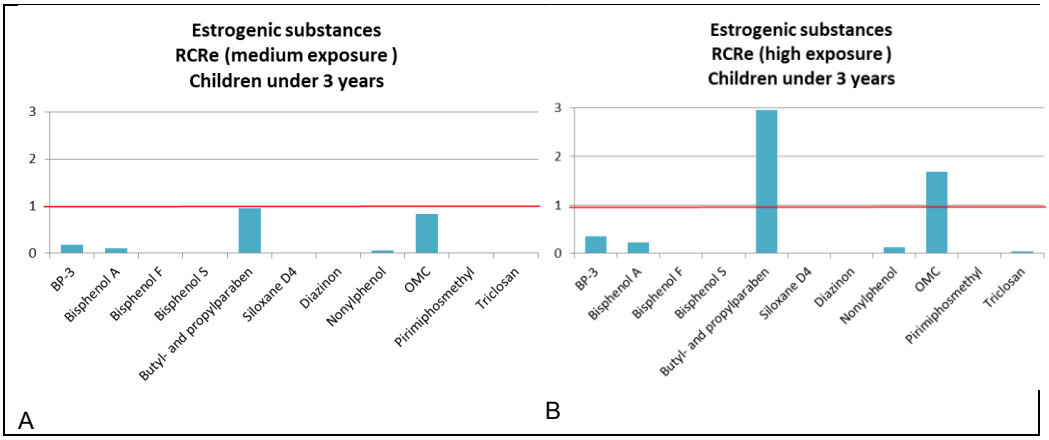


Figure 8.5. RCR E values for exposure of children under 3 years for individual substances with estrogenic effect. A indicates RCR E values calculated from medium exposures, while B indicates RCRe values calculated from the scenario with high exposures.

Pregnant women/ unborn children – medium and high exposure

For pregnant women/ unborn children, OMC, nonylphenol, butyl- and propyl paraben and BP-3 contribute most to the total RCRtotal_e (Figure 8.6). In addition to the two parabens (RCRe = 0.2) and nonylphenol (RCRe= 0.3), the UV filters BP-3 and OMC contribute with RCR E values of 0.1 and 0.4, respectively, for pregnant women/ unborn children in the scenario with medium exposures. It should be noted that this scenario includes the use of 18 g of sunscreen per day for OMC and BP-3, but no use of sunscreen for butyl- and propyl paraben. The scenario with high exposure includes the use of 36 g of sunscreen per day for OMC and BP-3 (Appendix 6c), and particularly butyl- and propyl paraben, OMC, nonylphenol, bisphenol A, BP-3 and siloxan D4 contribute to the total RCR total for high exposure. See detailed discussion of the sources of the individual substances below (Section 8.2.9).

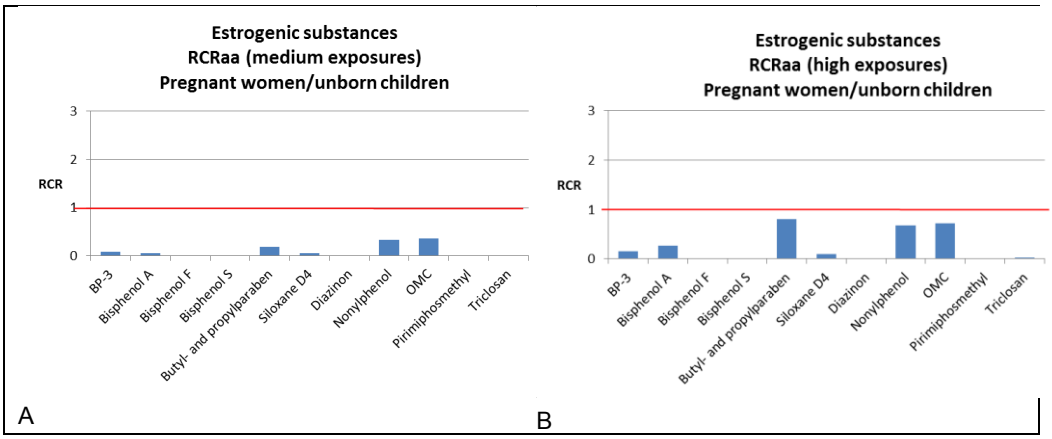


Figure 8.6. RCRe values for exposure of pregnant women/ unborn children for individual substances with estrogenic effect. A indicates RCRe values calculated from medium exposures while B indicates RCRe values calculated from high exposures.

For bisphenol A, a DNEL corresponding to EFSA's temporary TDI of 4 µg/kg /d is used in this project. DTU Food Institute has concluded that this TDI should be lower in order to take sufficient account of bisphenol A's endocrine disrupting effects on the development of breast tissue (DTU 2015b). By applying the lower DNEL of 0.7 µg/kg/d for bisphenol A, RCRe of bisphenol A is increased to 0.6 and 1.6 at medium and high exposure, respectively for children, while RCRe is increased to 0.3 and 1.3 at medium and high exposure, respectively, for pregnant women/ unborn children. Thus, bisphenol A contributes significantly to the overall RCRtotal for estrogenic substances already at medium exposure.

8.2.4 Thyroid hormone disrupting substances

It appears from figure 8.1 that RCRtotal for thyroid hormone disruption is higher than 1 for children and pregnant women/ unborn children in relation to both high and medium exposure (just above 1 for women/ unborn children at medium exposure).

Children under 3 years – medium and high exposure

Figure 8.7 shows a larger contribution from OMC (in sunscreen) for children, but also dioxins and PCBs, triclosan (indoor environment), BHA and BHT contribute significantly to the total RCRtotal_thyr (Figure 8.7). In the scenario with high exposure, RCRthyr is close to or above 1 for BHT, OMC and triclosan. For children, DEHP also contribute in connection with high exposure (RCR = 0.2).

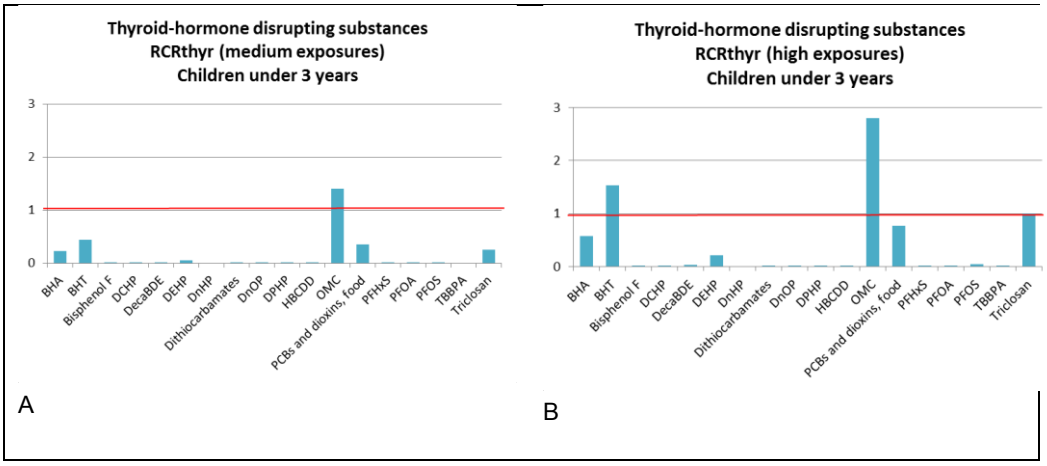


Figure 8.7. RCR values for exposure of children under 3 years to individual substances with thyroid hormone disrupting mode of action. A indicates RCR values calculated for medium exposures, while B indicates RCR values calculated for high exposures.

Pregnant women/ unborn children – medium and high exposure

Figure 8.8 shows a large contribution from OMC (in sunscreen) for pregnant women/ unborn children, but also BHA, BHT, dioxins and PCBs and triclosan contribute significantly to RCRtotal for thyroid disrupting effects at both medium and high exposure.

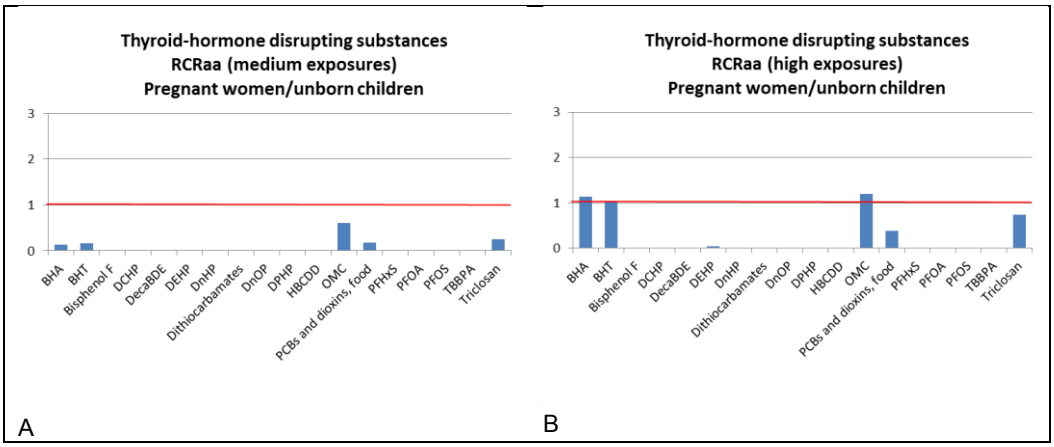


Figure 8.8. RCR values for exposure of pregnant women/ unborn children to individual substances with thyroid hormone disrupting mode of action. A indicates RCR values calculated for medium exposures while B indicates RCR values calculated for high exposures.

8.2.5 Risk Assessment in connection with analysed content of BHA and BHT in cosmetics

Two exposure scenarios are described in Section 6.6.1 using body lotion and sunscreen, respectively, containing BHT corresponding to the highest measured content in products analysed in this project. Especially BHT in sunscreen contributes to the overall risk as RCR values when using both body lotion and sunscreen result in RCR values of 0.3 and 0.2 for children under 3 years and pregnant women/ unborn children, respectively (Table 8.1).
It can be seen (Figures 8.7 and 8.8 and Appendix 8), that for the calculated exposures to BHT, the RCR-values for children and pregnant women/ unborn children are 1.5 and 1.0, respectively for the total exposure to BHT from cosmetics, food and indoor environment for the high exposure from food and the use of both sun lotion and sunscreen.

Table 8.1 RCR values for thyroid hormone disrupting effect of BHT at the exposure of children under 3 years and pregnant women/ unborn children. The values are calculated in relation to exposure from body lotion alone, and for body lotion together with sunscreen. Furthermore, the aggregated exposure is calculated by adding the values for medium and high exposures.

Age group	DNEL µg/kg/d	Exposure body lotion, µg/kg/d	Exposure body lotion and sunscreen, µg/kg/d	RCRthyr, body lotion	RCRthyr, body lotion and sunscreen
Children under 3 years	250	19.2	80.6	0.08	*0.32*
Pregnant women/ unborn children	250	12	50.4	0.05	*0.20*

8.2.6 Risk assessment in connection with analyses of bisphenol A and phthalates in pizza boxes

In this project, chemical analyses of pizza boxes were carried out for the content of bisphenol A and phthalates. Levels of bisphenol A and phthalates were measured in the pizza boxes at 50 % ethanol extraction corresponding to the total content in the cardboard, as the cardboard structure was degraded during the stay in the migration liquid. In contrast, migration above the analytical detection limit could not be measured from an intact cardboard surface from the

pizza box, using sampling in TENAX which is a powder-formed material used for simulating migration from dry food items.
The exposure scenarios in Section 6.6.2 indicate the exposure of children and pregnant women/ unborn children, respectively, if the contents of phthalates and bisphenol A were at the detection limit.
Phthalates and bisphenol A are not detected by the Tenax migration method and the exposure and the risk will therefore be lower than indicated in Table 8.2

Table 8.2 Exposure estimates for phthalates and bisphenol A at the detection limit and calculated RCR values for children and pregnant women/ unborn children. The substances are grouped by mode of action (aa: antiandrogenic; thyr: thyroid hormone disrupting; e: estrogenic mode of action), and the sum of RCR values within each substance group is inidcated. RCR values above 0.1 are shown in *italics*.

Substance	DNEL µg/kg/d	Exposure from pizza box with content at detection limit, children under 3 years µg/kg/d	Exposure from pizza box with content at detection limit, pregnant women/ unborn children µg/kg/d	RCR, children under 3 years	RCR, pregnant women/ unborn children
DEHP (aa)	35	1.2	0.5	0.034	0.014
DBP (aa)	6.7	1.2	0.5	*0.179*	0.075
DIBP (aa)	8.3	1.2	0.5	*0.145*	0.060
DINP (aa)	1500	12	5	0.008	0.0033
BBP (aa)	500	1.2	1	0.0024	0.0020
SUM (aa)				***0.36***	***0.15***
DEHP (thyr)	263	1.2	0.5	0.0046	0.0019
DNOP (thyr)	368	1.2	0.5	0.0033	0.0014
SUM (thyr)				**0.0078**	**0.0033**
Bisphenol A (e)	4	2.4	1	*0.60*	*0.25*
Bisphenol A* (e)	0.7	2.4	1	*3.4*	*1.4*

** For bisphenol A, calculations are also made with alternative, lower DNEL (DTU 2015), see Appendix 7a.*

Table 8.2 shows that for bisphenol A and the phthalates DBP and DIBP even content at the detection limit will result in RCR values above 0.1. Especially for bisphenol A, there may be cause for concern already with the content on the detection limit, as RCR exceeds 1 by use of the lower alternative DNEL.
If it is assumed that bisphenol A migrates out of the box at a level corresponding to the detection limit in the migration test, RCR values above 1 would be achieved for children under 3 years, who daily eat half a pizza (RCR = 0.6 and 3.4 using either the EFSA tTDI or an alternative DNEL) and for pregnant women who daily eat a whole pizza (RCR = 0.25,and 1.4, using either the EFSA tTDI or an alternative DNEL).

For DEHP, DINP, BBP and DNOP it can be concluded that there is no migration to an extent that gives rise to concern, as content is measured below the detection limit for migration to Tenax, and as even content at the detection limit is not considered to be of concern. As the contents of bisphenol A, DBP and DIBP at the detection limit will give rise to RCR values above 0.1, it is not known whether the migration of bisphenol A, DBP or DIBP occurs to an extent that gives rise to concern. Thus, there can be no conclusion as to whether there is a

risk of endocrine disrupting effects when eating pizza. Thus, development of analytical methods with lower detection limits will be required before a valid assessment of bisphenol A, DBP and DIBP can be made for this scenario.

8.2.7 Biomonitoring data

RCR calculated using exposure estimates based on biomonitoring data is given in Table 8.3 and Table 8.4 for children under 3 years and pregnant women/ unborn children, respectively. In order to compare results obtained using biomonitoring data with the exposure estimates based on content in food, indoor environment and consumer products, both RCR values for biomonitoring data and modelled exposure data are presented.

Table 8.3 shows that for children there is good agreement between RCR values calculated from biomonitoring data and RCR values calculated from the modelled exposure data for all phthalates. For PFOS, the RCR values based on biomonitoring data are higher than for modelled data, while RCR values based on biomonitoring data for BP-3, bisphenol A and parabens are lower than the RCR values based on biomonitoring data. Possible reasons for these differences are discussed for the individual substances in Section 8.2.9.

Table 8.3 Children under 3 years, RCR calculated for estimates based on biomonitoring data and modelled data

	Human biomonitoring					**Modelled data**	
Substance	**DNEL µg/kg/d**	**Medium exposure µg/kg/d**	**High exposure µg/kg/d**	**RCR medium**	**RCR high**	**RCR mdium**	**RCR high**
Antiandrogenic substances							
BBP	500	0.49	2.90	**0.0010**	**0.0058**	0.0008	0.0057
DBP	6.7	3.56	13.06	**0.53**	**1.9**	0.33	1.8
DEHP	35	4.77	19.7	**0.14**	**0.56**	0.35	1.6
DIBP	8.3	3.19	16.06	**0.38**	**1.9**	0.28	2.3
DINP	1500	2.3	9.1	**0.0019**	**0.0061**	0.0015	0.0061
PFOS	0.08	0.02	0.054 (worst case)	**0.25**	**0.68**	0.018	0.047
Estrogenic substances							
BP-3	9370	0.027	95-perc: 1.388	**0.000003**	**0.00015**	0.18	0.35
Bisphenol A	4	0.04-0.066 (median)	0.15-0.283 (95-perc)	**0.017**	**0.071**	0.097	0.28
Bisphenol A	0.7*	0.04-0.066 (median)	0.15-0.283 (95-perc)	**0.094**	**0.40**	0.55	1.58
Butyl- og propyl paraben	20	Propylparaben: 0.30	Propylparaben: 0.38	**0.015**	**0.019**	0.95	2.95
Thyroid hormone disrupting substances							
DEHP	263	4.77	19.7	**0.018**	**0.075**	0.047	0.21
PFOS	0.1	0.02	0.054 (worst case)	**0.20**	**0.54**	0.014	0.038

* For bisphenol A, an alternative DNEL has been calculated as well, see Appendix 7a.

Table 8.4 Pregnant women/ unborn children, RCR calculated for estimates based on biomonitoring data and modelled data.

	Human biomonitoring					Modelled data	
Substance	**DNEL µg/kg/d**	**Medium exposure µg/kg/d**	**High exposure µg/kg/d**	**RCR medium**	**RCR high**	**RCR mdium**	**RCR high**
Antiandrogenic substances							
BBP	500	0.13	0.47	**0.00026**	**0.00094**	0.0005	0.0017
DBP	6.7	0.543	1.34	**0.081**	**0.2**	0.13	0.44
DEHP	35	1.56	5.12	**0.045**	**0.15**	0.12	0.37
DIBP	8.3	1.66	3.04	**0.2**	**0.37**	0.098	0.33
DINP	1500	0.75	5.50	**0.0005**	**0.0037**	0.00031	0.0015
Estrogenic substances							
Bisphenol A	4	0.03-0.04	95-perc: 0.13-0.24	**0.01**	**0.06**	0.054	0.27
Bisphenol A	0.7*	0.03-0.04	95-perc: 0.13-0.24	**0.06**	**0.34**	0.31	1.52
Triclosan	750	0.49	90-perc: 0.565	**0.00065**	**0.00075**	0.0097	0.029
Thyroid hormone disrupting substances							
DEHP	263	1.56	5.12	**0.0059**	**0.019**	0.016	0.049
Triclosan	30	0.49	90-perc: 0.565	**0.016**	**0.019**	0.24	0.73

* For bisphenol A, an alternative DNEL has been calculated as well, see Appendix 7a.

Table 8.4 shows that for pregnant women/ unborn children there is good agreement between RCR values calculated from biomonitoring data and RCR values calculated from the modelled exposure data for all phthalates. RCR values based on biomonitoring data for bisphenol A and triclosan are lower than RCR values based on biomonitoring data. Possible reasons for these differences are discussed for each substance in Section 8.2.9.

8.2.8 Discussion of assessment of endocrine disruptors

The risk assessment shows that a number of substances with antiandrogenic, estrogenic or thyroid hormone disrupting modes of action each can be associated with a risk for high exposed children and pregnant women/ unborn children as the risk characterisation ratio (RCR) is higher than 1 for several individual substances. As described above, RCR describes the relationship between exposure and a tolerable exposure dose (DNEL) and RCR will be higher than 1 when exposure exceeds DNEL.

For children and pregnant women with medium exposure, RCR for most substances is below 1 and does not indicate any risk for exposure to each individual substance. However, RCR values close to or above 1 are seen for children for the following individual substances: dioxins and dioxin-like PCBs (RCRaa = 1.1), butyl and propyl paraben (RCRe = 0.95) and OMC (RCRthyr = 1.4). However, looking at the overall risk of the grouping of substances with the same modes of action, the calculation shows total RCR values above 2 for children and close to or above 1 for pregnant women/ unborn children, suggesting that even at medium exposures, the risk from these substances is not controlled.

Uncertainties are associated with the calculation of RCR values both for exposure estimates and for DNEL determination. For exposure data, the major uncertainties are considered to be for substances with exposure via consumer products, as it is very important how these products are used, whether they are used, and very dependent of the content of a given substance and its potential for migration from the product. For example, there is large difference in the

result depending on whether sunscreen is included or not in the assessment. Generally, for substances in cosmetic products and other consumer products there is uncertainty concerning the exposure estimate due to lack of knowledge regarding the actual content of a substance, and also there is great individual variation in exposure. Furthermore, the validity of the exposure data may vary considerable from exposure source to exposure source for a substance, depending of the reliability of the data. For example, data regarding content of chemicals in food are considered well determined, while exposure from indoor environment is less well determined.

In relation to DNEL determination, there is uncertainty by using a traditional risk assessment method for endocrine disruptors, as it is an ongoing discussion whether there is a threshold value for endocrine disrupting effects. Presumably, a calculation of RCR that does not require a threshold value will lead to higher RCR. The impact of this uncertainty is not assessed further in this project. In addition, the uncertainty is highest for the substances where only a few studies have investigated endocrine disrupting effects, and dose selection and endpoint in each study are of great importance for the size of DNEL.

8.2.9 Discussion of findings for individual endocrine disruptors

In the following, we go through the calculated results for each group and the uncertainties associated with the individual RCR values (in addition to the general ones, as described above). The focus is particularly on the substances found to pose the highest contribution to endocrine disrupting effects (i.e. those having the highest RCR values). Particularly interpretation and uncertainties are discussed relating to:

- RCR values
- exposure sources and estimates
- hazard assessment and DNEL value
- biomonitoring data
- lack of knowledge

In the discussion of exposure sources and DNEL values, the information provided in Appendices 6a and 7a for the specific substances is particularly referred to.

Paracetamol contributes with by far the largest RCRaa values. In scenarios for medium and high exposure (i.e. by daily intake of 25 % and 100 %, respectively, of the maximum recommended daily dose during a vulnerable period in early development) the RCRaa values are 25 and 100, for children, and 33 and 133 for pregnant women, respectively (Appendix 8). This indicates a potential risk of antiandrogenic effects at such exposure during critical periods during development. At present, it is not clear when during development, or how long such an exposure would contribute to a risk for adverse effects later in life. These RCRaa values far exceed the RCR values for the other substances. Again, it should be noted that paracetamol is different from the other substances and risk assessment of medicinal products as a starting point will be different from the risk assessment of chemicals from food, cosmetics, indoor environment, as this medical agent is developed for at specific purpose (pain relief). Thus, there may be acceptable side effects associated with the therapeutic use and therefore, well-defined recommendations apply for the product use especially when it comes to treatment of pregnant women and children.
It has not been possible to estimate the consumption of paracetamol among pregnant women and children below 3 years as this product is sold as a non-prescribed medical product. It is to be assumed that a small fraction of these groups use paracetamol during a critical period of development of the fetus/ small child and that the duration of the treatment reflects the recommendation of the medical authorities. In appendix 4 a questionnaire is referred in which it is shown that 0.2 % of pregnant women used paracetamol every day. However, the intake of paracetamol for medical purpose can be controlled by the consumer, which might not be the case for the other substances mentioned in this report.

For paracetamol, we calculate DNEL and RCR values following the same principles as for the environmental or food-related substances in order to get an overall view of the risk for the endocrine disrupting effects from all sources and their relative contribution. Thus, it can be seen that by using the same risk assessment approach as for other products, paracetamol is a major contributor to the overall risk of endocrine disrupting effects for the persons who use this medicinal product at a critical time. As noted, the risk assessment is performed with other methods than by normally done for medicinal products. The risk assessments of endocrine disrupters in this project are performed on the basis of results in animal experiments, and for all of the substances assessment factors are applied in order to estimate a tolerable exposure level for humans. In this project an overall assessment factor of 100 is generally used in order to consider for differences between animals and humans and individual differences among the susceptibility in humans. The Danish Medicines Agency states that for medical products such assesment factors are not normally used, as generally much more data are available on exposure and associated effects from thousands of people at the dose levels used in humans. Higher doses of paraccetamol than recommended can cause serious poisoning, especially liver damage, and these are seldom seen. However, it is not all types of effects that can be determined in experimental animals that also are examined for in humans e.g. hormone disruption.

Effects of paracetamol on androgenic sensitive endpoints have been seen in experimental animals. This points to an antiandrogenic mode of action, and the DNEL for Paracetamol is considered robust. Besides these signs for antiandrogenic mode of action, epidemiological studies in Denmark and other European countries have shown an association between intake of paracetamol early in pregnancy and increased risk for cryptorchidism (Jensen et al. 2010, Snijder et al. 2012), while other studies have found associations between intake of paracetamol and other types of analgetics and short anogenital distance in boys (Lind et al. 2016; Fisher et al 2016). These findings point towards that paracetamol also in humans may have an antiandrogenic mode of action during pregnancy. However, other studies have not found these associations and also no association has been found for hypospadia.

In Europe, the suspected hormone disrupting (antiandrogenic) effects of paracetamol have been discussed at several occasions. The Danish Medicines Agency reports that in connection with discussions in the European Medicines Agency, the Pharmacovigilance Working Party and Pharmacovigilance Risk Assessment Committee (PRAC) it was evaluated that at present and based on the available data there is not sufficient evidence for an association between paracetamol and antiandrogenic effects. Both the experimental animal studies as well as epidemiological studies indicating such an association were considered too weak for concluding a causal relationship.

The Danish Medicines Agency emphasises that when use of analgesics is needed during pregnancy then paracetamol is still recommended compared to other non-prescribed analgesics, as paracetamol is considered the least harmful for unborn children. Also, it is recommended that paracetamol only should be used when there is a medical need and at lowest dose levels and for shortest duration, which is the general recommendation for all types of medical products used during pregnancy.

Dioxins and dioxin-like PCBs contribute significantly to the total RCRaa and RCRthyr values. In the scenario with medium exposures, particularly foods that contribute (figure 8.3 and 8.4) and the results (RCRaa = 1) indicate a potential risk for children exposured to dioxins and dioxin-like PCBs in foods alone. In the scenario with high exposure where RCRaa values are well above 1 for children, the indoor environment contributes significantly, as exposure through indoor dust in PCB-contaminated housing is included (Figure 8.3). As described in Chapter 7 (hazard assessment), TEQ-based values are used for the PCBs/ dioxins in foods, and both exposure as well as DNEL values are TEQ-based. PCBs in indoor dust are based on measurements of PCBtotal (selected indicator PCBs called PCB6 or PCB7) and DNEL is based on PCB mixtures. Data on PCBs in indoor air are not included in the RCR calculations for hormone disruption, as no adequate data were found for establishing a DNEL in relation to these volatile PCBs. Exposure form indoor air may nevertheless be a potential source for PCB-exposure and thus, the overall risc in PCB-contaminated housing may be underestimated.

The exposure estimate for children's intake via foods is based on Danish data and is found to be robust (Appendix 6a). The exposure estimate for dust is based on PCB measured in in a school building, however, there is considered to be great variations in indoor dust levels and human exposure. No useful estimates based on biomonitoring data were found for comparison with the calculated values. Data on PCB in breast milk (appendix 6a) indicates a PCB exposure of infant nursed by their mother. However, there are significant advantages by nursing the child that are considered to outweigh the potential risk from the PCB content in the milk.

DNELaa and DNELthyr for the dioxins and dioxin-like PCBs in foods (based on the calculation of TEQ, see Chapter 7) are also considered as robust. DNEL for PCBtotal in indoor dust is less robust since it is based on studies of monkeys dosed with mixtures of PCBs (dioxin-like and non-dioxin-like), and there may be significant differences between the PCB compositions to which persons are exposed and the mixtures used in the animal studies.

For **the phthalates**, DEHP, DBP and DIBP are particularly seen to contribute significantly to the RCRtotal values for antiandrogenic effect, and these three phthalates contribute overall to an RCRaa near 1 for children at medium exposure and an RCRaa near 6 at high exposure. For these phthalates, there are good exposure data, and there is good agreement between calculated exposure values and estimated values based on biomonitoring studies. Foods, consumer products and indoor environment contribute to children's exposure to these phthalates (see Table 6.1). For DBP and DEHP, DNEL for antiandrogenic effect can be considered robust, but as DIBP has not been studied to the same extent as DEHP and DBP, there is some uncertainty associated with the DNEL for DIBP. This project used a low (i.e. cautious

or conservative) DNEL for DIBP based on similarities between DBP and DIBP in terms of structure and toxic properties.

For thyroid hormone disrupting effects, DEHP contributes slightly with RCRthyr = 0.2 in the scenario with high exposure, where the sources are foods, indoor environment and consumer products.

DEHP, DBP and DIBP are among the phthalates, to which children and adults are mostly at risk, but also for BBP and DINP relatively high exposure levels are seen. Because BBP and DINP have higher DNEL values than DEHP, DBP and DIBP for antiandrogenic effect, they contribute only marginally to the total RCRaa. For other phthalates, for example DnOP, DPHP and DHCP, the exposure is low. The calculated exposure values for these phthalates include only data for intake from foods, as there is generally limited knowledge on exposure from other sources, such as consumer products, and a lack of biomonitoring data. As the use of e.g. DEHP and DBP is decreasing, and as especially DINP and DnOP are seen as possible alternatives it is likely that human exposure to these other phthalates will increase with time. Also for these phthalates, data used for DNEL determination for antiandrogenic effect can be considered relatively robust, although there are limited studies of hormone-sensitive endpoints. For thyroid hormone disrupting effects, there are only a few animal studies as well, and there is some uncertainty about the DNELthyr determination for phthalates.

Bisphenol A contributes to the RCR values for estrogenic effect, and as can be seen from Table 6.1 (Chapter 6), the bisphenol A exposure of children in this scenario originates particularly from foods and consumer products. Exposure data for bisphenol A from foods and other sources are considered valid. Biomonitoring based exposure estimates for bisphenol A (and thus RCR values) are approximately one fifth of the exposure values calculated from the content in foods and products. This difference is not large relative to the individual differences and methodological uncertainties associated with exposure estimates and risk assessments. As mentioned, the DNEL for bisphenol A is controversial, and here the EFSA temporary TDI of 0.4 µg/kg/d is used. Use of a lower DNEL would result in RCRe values above 1 in the most exposed individuals (RCRe values of 1.6 and 1.3, respectively, for children and pregnant women, see Tables 8.5 and 8.6). Also at medium exposure bisphenol A contributes significantly to the total RCRe, if the lowest DNEL is used (RCRe of 0.6 and 0.3 for children and pregnant women, respectively). Exposure to bisphenol A in pacifiers would further contribute with a RCRe of 0.06 with the TDI value from EFSA and of 0.33 by the use of the lower, alternative DNEL.

Exposure data show lower intake of **bisphenol F and S** through foods than of bisphenol A, and exposure data for other sources for bisphenol F and S or biomonitoring data are not found. Future replacement of bisphenol A with other bisphenols may increase exposure to analogs as bisphenol F and S. The determination of DNELs for bisphenol F and S is based on few experimental studies, and it is unclear whether DNELs would be lower if other hormone sensitive endpoints were tested for bisphenol F and S. Overall, RCR for bisphenol F and S is associated with significant uncertainty.

Nonylphenol contributes only a little to the total RCR for children, but is seen to contribute significantly to the total RCR for pregnant women/ unborn children (RCR = 0.3 at medium exposures and RCR = 0.7 at high exposures). Exposure is from clothing and to a lesser extent from foods. According to Danish EPA 2012, data are lacking on migration of nonylphenol and nonylphenol ethoxylates from clothing and due to this there is significant uncertainty associated with RCR for nonylphenol, although DNEL determination is considered fairly robust. For children, exposure values for nonylphenol are based on individual studies of content in drinking water and soil, while data on exposure from clothing are not included. There were no relevant biomonitoring data for comparison.

BHA and BHT in foods contribute to some extent to RCRthyr at medium exposures, but contribute significantly to RCRthyr in the scenario with high exposures. Here the RCR values for children and pregnant women/ unborn children are near 1 (slightly above or slightly below) suggesting that the risk of endocrine disrupting effects may not be controlled for individuals with high intake. The exposure figures for BHA and BHT used as food additives originate from EFSA and are considered relatively robust, but as exposure to BHA and BHT used in the packaging is not included, it is possible that the total exposure to BHA and BHT in foods is underestimated.

BHA and BHT measured in cosmetics in this project show that there are few products containing BHA (one body oil), but more containing BHT at concentrations up to 0.32 % in sunscreen and 0.23 % in body lotion. There is insufficient knowledge about the absorption of BHT through the skin, but to calculate the RCR values, we have used a maximum dermal absorption rate of 4 %, according to data from Cosmetic Ingredient Review (2002). It is seen that BHT in cosmetic products potentially contributes to the overall RCRthyr, as RCR values by use of body lotion and sunscreen (at high exposure) will result in RCRthyr values for BHT of 0.3 and 0.2 for children and pregnant women/ unborn children, respectively. Although there is some uncertainty about the dermal absorption of BHT, it is likely that BHT in cosmetics may contribute to a lesser extent to the overall risk of the thyroid hormone disrupting effect. DNELthyr for BHT is considered relatively robust and corresponds to the EFSA ADI. For BHA, the DNELthyr determination is assessed to be less robust (see Appendix 7a).

Triclosan contributes to some extent to RCRthyr at medium exposures, and significantly to RCRthyr in the scenario with high exposures for children under 3 years and pregnant women/ unborn children (RCR Thyr 1 and 0.7, respectively). RCRe for triclosan is low for children and pregnant women/ unborn children in both scenarios. In the scenario with low exposures, triclosan exposure originated especially from indoor environment (dust) for children and from consumer products (toothpaste) for adults. Focus has not previously been on the fact that triclosan in dust is found to contribute significantly to the risk of endocrine disrupting effects in children. The exposure calculation for children's intake via dust is based on a Belgian study from 2009 and is considered relatively robust, and as reference is made to other relevant data with similar content in the dust, the exposure values are generally considered reliable (Geens et al., 2009). The exposure of adults via toothpaste with triclosan is well known, and there is currently only one toothpaste on the market containing triclosan. Knowledge is still lacking about the exposure of children and adults to triclosan from other applications, e.g. in clothing and in food contact materials, etc. There is no useful biomonitoring data for children, but for adults lower exposure estimates based on biomonitoring are seen compared with calculated exposure. DNELthyr for triclosan is considered relatively robust while DNELe is less robust.

For **butyl and propyl paraben**, the basis scenario is based on daily use of creams/ cosmetics containing the maximum limit value, while the scenario with high exposure also includes use of sunscreen with a maximum content of these parabens. It is not clear whether these substances are typically used in the maximum allowable concentrations, and it should be noted that a lower content would result in lower RCR values. There are no relevant biomonitoring data for comparison with the modelled values for adults via cosmetic products. For children, the exposure estimates based on biomonitoring (and thus the RCR values) is of about 1/100 of estimates based on modelled estimations values. However, it is important to bear in mind that the modelled exposure estimates are calculated for users of creams with the maximum permitted content of butyl or propyl paraben. Biomonitoring data cover a broader group of children, and it must be assumed that very few children have used cream containing these parabens, and that such large amounts of cream, which are part of the modelled values, are not always used (see Appendix 6a). In Denmark, it is not allowed to use butyl and propyl paraben in cosmetics intended for children. This is not reflected in the calculations, where it is assumed that children may use creams not specified for children, and thus the exposure estimates may be overesti-

mated. Data for intake of propyl paraben via breast milk have been found, and these data suggest that a possible contribution from the breast milk is significantly less than the estimated exposure via the skin. There is some uncertainty about the NOAEL determination, and due to limited knowledge about the differences in uptake and metabolism between animals and humans, for butyl and propyl paraben there is additional uncertainty in DNEL determination.

For the UV filters **BP-3 and OMC**, the basic scenario is based on daily use of 18 g sunscreen while the scenario with high exposure uses 2x18 g sunscreen daily and the content of UV filters are set at the regulatory limits 6 and 10 %, respectively. It is not clear whether these substances are typically used in the maximum allowable concentrations, and it should be noted that a lower content will result in lower RCR values. It can be assumed that children and pregnant women are only exposed to such high amounts of sunscreen for limited periods, and that on average smaller amounts of sunscreen are used. It should be noted that during sensitive periods in early development, short-term high exposure to endocrine disruptors might cause permanent effects or effects later in life. Only biomonitoring data for BP-3 have been found in Danish children, and these data suggest much lower exposures than the calculated exposure data, but as measurements in children have been made in the autumn, it is likely that children's exposure would be higher in the summer months. There are no robust experimental data for the endocrine disrupting potential for BP-3, and the DNEL determination is uncertain. For OMC, there are robust experimental data suggesting endocrine disrupting potential for oral exposure of rats to the substance, but as human exposure occurs via the skin, there is some uncertainty about the relevant DNEL determination.

For **siloxane D4**, the exposure does not give cause for concern, as the RCR values for pregnant women/ unborn children are 0.05 and 0.1, respectively, at medium and high exposure. However, there is some uncertainty associated with the exposure data, as data from different reports (Danish EPA 2012a and SCCS 2010) use somewhat different values for the content of siloxane D4 in cosmetic products. In this project, the data from Danish EPA (2012a) are used. In the scenario with medium exposures, the exposure value for pregnant women/ unborn children is determined for products other than sunscreen, and at high exposures, the calculation includes the use of sunscreen. The products measured in Danish EPA (2012a) showed a rather low content of D4 (0.34 %). Due to the findings in this survey a content of 0.003 % was used for other cosmetic products, i.e. a difference of a factor of 100. In SCCS opinion from 2010, 7.8 % content of siloxane D4 is assumed in creams, which would lead to a 23-fold higher exposure number and thus an RCR value of 2.3 in the scenario with the use of sunscreen. Such high levels of siloxane D4 would cause concern when used in large quantities, e.g. in sunscreen.

There is no biomonitoring data available for comparison with the calculated exposure data. Data for endocrine disrupting effect of siloxane D4 can be considered robust, but as the starting point is a study of exposure via inhalation, there is some uncertainty about DNEL determination and conversion of exposure from external to internal doses for animals and humans.

The perfluorinated substances and the brominated flame-retardants are not seen to contribute significantly to RCRtotal for any of the effect groups. However, RCR of 0.01 to 0.05 is seen for several of these substances, which shows that they contribute to some extent to the overall RCRtotal. These substances are probably just a few examples from a larger group of substances with the same modes of action and the same use, although in this project we have not found data suitable for cumulative risk assessment for all of these substances. For both perfluorinated and brominated substances, there is a lack of data on both exposure and toxicity, and there is some uncertainty due to differences in metabolism in animals and humans. Therefore, there is large uncertainty for the RCR values for these substances. It should be noted that when determining the DNEL for some of the substances, accumulation in biological tissue was taken into account. This is not the case for the other substances (see detailed hazard assessment in Appendix 7a).

For **PFOA and PFOS**, the scenarios with medium and high exposures show very low RCR values for children and pregnant women/ unborn children. Furthermore, specific scenarios are indicated in Chapter 6 which are worst-case scenarios using the highest value from he range of 95-percentiles for PFOS and PFOA exposure from foods in Europe. These values are three to seven times higher than the exposure values for high exposures based on Danish and Swedish data regarding content in foods (Tables 6.1 and 6.3). If these absolute worst-case values are used to calculate RCR, RCRthyr and RCRaa for PFOS will result in RCR values of 0.13 and 0.16 for children and of 0.068 and 0.085 for pregnant women/ unborn children, respectively. This suggests that some children and pregnant women may be exposed to high PFOS amounts that may contribute to the overall risk of endocrine disrupting effects. Also, PFOS in breast milk as found in a German study may contribute to the hormone disrupting effects as RCRthyr and RCRaa for PFOS in breast milk and nursing of children are estimated to 0.20 and 0.54, respectively. There is some uncertainty associated with both DNEL determination and exposure values.

The pesticides diazinon, linuron, pirimiphosmethyl, procymidone and dithiocarbamates contribute very little with RCR values of no more than 0.01. However, this report only uses average values for exposure from food. This may cause underestimation of the risk as higher intake in certain population groups and for shorter or longer periods is likely. Especially when it comes to risk of endocrine disrupting effects in sensitive periods, such short-term, but high intake can be of concern. Because there are good Danish data for individual exposure to pesticides, it may be relevant in any future projects to make more accurate risk assessments based on data from e.g. selected foods or population groups. However, such detailed assessments are not covered by this project.

It should also be noted that a number of pesticides/ biocides are omitted because of low exposure from foods, but people may be exposed to some of these substances from other sources, such as from home use. Thus, there is some uncertainty linked to the exposure estimates for pesticides. For the included pesticides, there are good data showing endocrine disrupting potential, but the DNEL determination cannot be considered conclusive because of limited studies of hormone-sensitive endpoints. As currently work on cumulative risk assessment of pesticides/ biocides is taking place in EU context, the focus of this project is not to include many pesticides, but to focus on the pesticides most likely to contribute to RCR via intake through foods.

8.2.10 Overall assessment of sources contribution to the risk for endocrine disrupting effects

8.2.10.1 Most important substances

Children under 3 years

Table 8.5 indicates the substances considered the most important (i.e. the highest RCR values) for endocrine disrupting effects related to exposure of children under 3 years.

Table 8.5 Overview of endocrine disruptors' contribution to RCR (medium and high exposure) and sources of exposure of children under three years. SUM indicates RCRtotal for antiandrogenic, estrogenic and thyroid hormone disrupting substances, respectively. RCR values above 0.1 for individual substances are indicated in *italics*.

Antiandrogenic substances			
Substance	**Sources**	**RCR (medium exposure)**	**RCR (high exposure)**
Chlorinated substance			
PCBs and dioxins	Foods	*1.1*	*2.3*
PCBs and dioxins	Indoor environment	0	*0.45*
Phthalates			
DEHP	Foods, indoor environment, products	*0.35*	*1.6*
DBP	Foods, indoor environment, products	*0.33*	*1.8*
DIBP	Foods, indoor environment, products	*0.28*	*2.3*
Substance	**Sources**	***RCR (medium exposure)***	***RCR (high exposure)***
Medicine			
Paracetamol	Medicine	*25*	*100*
Sum: RCRtotal_aa (with paracetamol)		**27**	**117**
Sum: RCRtotal_aa (without paracetamol)		**2.1**	**17**
Estrogenic substance			
Parabens			
Butyl- and propyl paraben	Cosmetic products	*0.95*	*2.95*
Phenoler			
Bisphenol A	Foods, consumer products	0.097	*0.22*
Bisphenol A* (alternative DNEL)	Foods, consumer products	*0.55*	*1.25*
Nonylphenol	Foods, indoor environment	0.053	*0.13*
UV-filters			
BP-3	Cosmetic products (sunscreen)	*0.18*	*0.35*
OMC	Cosmetic products (sunscreen)	*0.840*	*1.68*
Sum: RCRtotal_e		**2.1**	**5.4**
Thyroid hormone disrupting substances			
Antioxidants			
BHA	Foods	*0.23*	*0.57*

BHT	Foods, cosmetics	*0.44*	*1.5*
Chlorinated substances			
PCBs and dioxin	Foods	*0.35*	*0.77*
Phthalates			
DEHP	Foods, indoor environment, products	0.047	0.21
UV-filters			
OMC	Cosmetic products (sunscreen)	*1.4*	*2.8*
Other substances			
Triclosan	Indoor environment	*0.25*	*1.0*
Sum: RCRtotal_thyr		**2.8**	**7.0**

* For bisphenol A is also indicated RCR values calculated using alternative, lower DNEL (DTU 2015, see Appendix 7a).

Pregnant women/ unborn children

Table 8.6 indicates the substances considered the most important for endocrine disrupting effects associated in relation to exposure of pregnant women/ unborn children.

Table 8.6 Overview of endocrine disruptors' contribution to RCR (medium and high exposure and individual scenarios) and sources to exposure of pregnant women/ unborn children. SUM indicates RCRtotal for antiandrogenic, estrogenic and thyroid hormone disrupting substances, respectively. RCR values above 0.1 for individual substances are indicated in *italics*.

Antiandrogenic substances			
Substance	**Sources**	**RCR (medium exposure)**	**RCR (high exposure)**
Chlorinated substances			
PCBs and dioxin	Foods	*0.53*	*1.15*
Phthalates			
DEHP	Foods, indoor environment, products	*0.12*	*0.37*
DBP	Foods, indoor environment, products	*0.13*	*0.44*
DIBP	Foods, indoor environment, products	0.098	*0.33*
Medicine			
Paracetamol	Medicine	*33.3*	*133*
Sum: RCRtotal_aa (with paracetamol)		**34.2**	**142**
Sum: RCRtotal_aa (without paracetamol)		**0.9**	**8.4**
Estrogenic substances			
Parabens			
Butyl- and propyl paraben	Cosmetic products	*0.19*	*0,8*
Phenoler			
Bisphenol A	Foods, products	0.054	*0,267*
Bisphenol A* (alternativ DNEL)	Foods, products	*0.31*	*1,52*
Nonylphenol	Foods, products	*0.34*	*0,68*
UV-filters			
BP-3	Cosmetic products	*0.077*	*0,15*
OMC	Cosmetic products (sunscreen)	*0.36*	*0,72*
Other substances			
Siloxane D4	Cosmetic products	0.052	*0,11*
Sum: RCRtotal_e		**1.1**	**2.8**

Substance	Sources	RCR (medium exposure)	RCR (high exposure)
	Thyroid hormone disrupting substances		
Antioxidants			
BHA	Foods	*0.13*	*1.14*
BHT	Foods, cosmetics	*0.17*	*1.0*
Chlorinated substances			
PCBs and dioxin	Foods	*0.18*	*0.38*
UV-filters			
OMC	Cosmetic products (sunscreen)	*0.6*	*1.2*
Other substances			
Triclosan	Toothpaste	*0.24*	*0.73*
Sum: RCRtotal_thyr		**1.3**	**4.6**

** For bisphenol A is also indicated RCR values calculated using alternative, lower DNEL (DTU 2015, see Appendix 7a).*

8.2.10.2 Knowledge base

The above overview of the substances that mostly contribute to the overall risk for endocrine disrupting effects indicates that for several substances there is lack of knowledge about human exposure, as well as knowledge on the toxic effects. Further knowledge in these areas could reduce the uncertainty of the assessments. It is estimated that the best documentation regarding knowledge about the effects and exposure levels is seen for the following substances: paracetamol, dioxins and PCBs, phthalates, bisphenol A and BHT. For BHT, in addition to contributions from foods, significant exposure from body lotion and sunscreen may occur according to measurements in this project (see Table 8.1).

It is clear that for substances in cosmetic products, uncertainty is associated with the exposure estimate, and there are large individual variations in the exposure.

8.2.10.3 Regulation

Consumers can control the intake of paracetamol. Dioxins and PCBs occur as pollutants (e.g. from incineration and from former use of PCB in building materials) and is therefore difficult for consumers to avoid from e.g. from foods. However, there are limit values for dioxins and PCBs in a variety of foods, such as fish, meat, eggs and dairy products. The main sources of dioxins in the Danish diet are wild fatty fish, dairy products and fat from meat. The Food Administration advices, however, particularly pregnant women to eat different kinds of fish, that is both fat and lean fish, and to reduce the intake of Baltic salmon as they may contain high levels of the substances. Regulation concerning PCBs in buildings is intended to protect the population although it is difficult for citizens/ users to clarify a possible risk. The phthalates that contribute with the highest RCR values (DEHP, DBP, DIBP) are regulated for use in food contact materials and articles for small children and in toys. The substances is however, still used in other consumer products and this may result in exposure form these products and from the indoor environment. Denmark in cooperation with the European Chemicals Agency has proposed a regulation of DEHP, DBP, DIBP and BBP in a number of consumer products. Bisphenol A is restricted for use in some types of materials, i.e. food contact materials and toys for small children and toys intended to put in the mouth. For e.g. BHT used as an additive, it is clear from the cumulative approach to risk assessment that although the exposure from foods is less than DNEL (ADI) for the substance itself (see EFSA 2012), the contribution to an overall risk of thyroid hormone disrupting effects may be important.

8.2.10.4 Grouping

The grouping of the substances was based on the three groups of endocrine disrupting effects; antiandrogenic effects, estrogenic effects and thyroid effects. However, in a cumulative risk assessment it would be relevant to assess the antiandrogenic and estrogenic substances together, as several of the substances affect the same endpoints in animal studies. As shown in Figure 8.2, an overall grouping of antiandrogenic and estrogenic substances results in a substantial increase of RCRtotal. There is inherently an increased uncertainty associated with the overall RCRtotal when grouping substances with different modes of action.

It may be discussed how large part of the population that would be exposed to high exposure levels of all substances simultaneously. In this project, it is clear that within each type of effects (antiandrogenic, estrogenic, thyroid effects) the substances are related and can originate from the same sources of exposure. For the group of substances with estrogenic mode of action, sunscreen can be the source of several substances (butyl and propyl paraben, UV filters, siloxane D4), and hence there is high probability of simultaneous exposure to these substances to users of sunscreen. For the group of substances with antiandrogenic mode of action e.g. the phthalates (DEHP, DBP and DIBP) contribute, and it is considered likely that the same people are exposed to high levels of these phthalates as biomonitoring studies show a high correlation between these phthalates in the same people (Frederiksen 2013). For the group of thyroid hormone disrupting substances, there are more diverse sources of exposure to the substances that contribute most to RCRtotal and it is not clear how likely it is that individuals are exposed to high exposure levels for these particular substances simultaneously.

8.3 Risk of chronic neurotoxic effects

Tables with all the RCR values for chronic neurotoxic effects related to the exposure scenarios for children under 3 years and pregnant women/ unborn children are shown in Appendix 8 in Tables 8G and 8H. The calculated RCR values and most significant findings are presented and discussed.

8.3.1 Cumulative risk assessment for neurotoxic substances (RCR_{total})

One objective of the project, in addition to assessing the possible risk for chronic neurotoxic effects for each substance, is to assess the overall risk related to exposure from several neurotoxic substances at the same time. In Section 7.1.2, justification is made for using an additive approach when assessing such an overall risk.

Figure 8.9 below shows the total RCR values that can be obtained when the RCR values for the individual neurotoxic substances and scenarios are added.

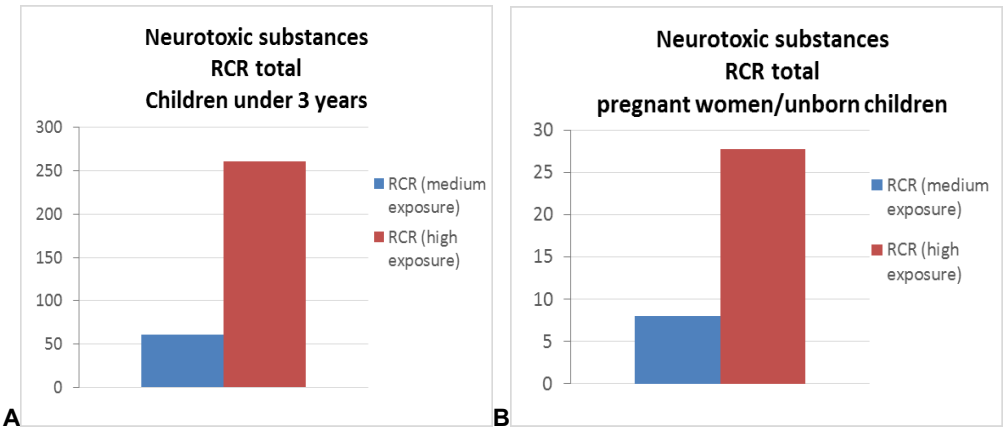


Figure 8.9. Total RCR values (RCRtotal) for simultaneous exposure to neurotoxic substances for A: children under 3 years and B: pregnant women/ unborn children.

Children under 3 years

When the RCR values for the 28 neurotoxic substances/ substance groups with calculated RCR values are added, an overall RCR value of 61.1 will be achieved from the medium exposure to all substances. Although it seems unlikely that a child would be exposed to all substances simultaneously, it is inevitable that this will actually happen for several of the substances, especially when taking into account that many of the substances with high RCR values occur in the same source of exposure - foods (see discussion of the individual substances in Section 8.3.7). This and simultaneous exposure contributions from other sources indicate that children under 3 years are generally exposed to neurotoxic substances at levels that significantly exceed the tolerable level for these effects.

When the RCR values for high exposure to all substances are added, a total RCR of 261 is achieved. This value cannot be regarded as realistic as it is considered unlikely for a child to be exposed at a high level to *all* substances simultaneously. Nevertheless, it must be assumed that for certain highly exposed children, it is not inconceivable that simultaneous exposure to only a few substances would result in very high RCR values.

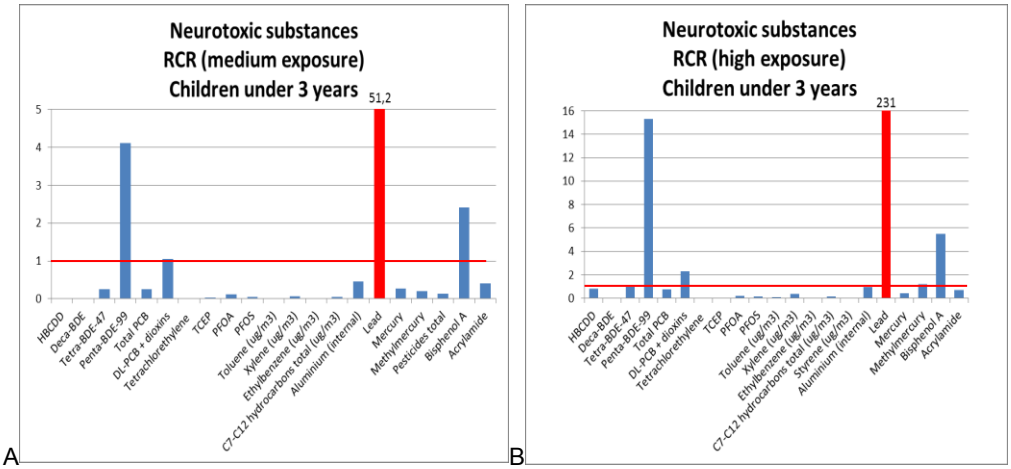
Pregnant women/ unborn children

When all the RCR values for the 28 neurotoxic substances/ substance groups at medium exposure are added, an overall RCR value of 7.9 will be achieved. This indicates that also pregnant women/ unborn children generally must be considered to be exposed to neurotoxic substances at levels that exceed the tolerable level.

Also for pregnant women/ unborn children, it must be assumed that the proportion of pregnant women may have high exposure to several of the substances simultaneously, and thus achieve significantly increased RCR values.

8.3.2 Individual substances, children under 3 years

Below in figure 8.10, RCR values for the individual neurotoxic substances are given in bar charts for medium and high exposure for children under three years:



A B

Figure 8.10 Children under 3 years, RCR values for the individual neurotoxic substances at medium (A) and high (B) exposure. The red bars indicate that the column goes beyond the diagram. The value is shown above the column.

Medium exposure

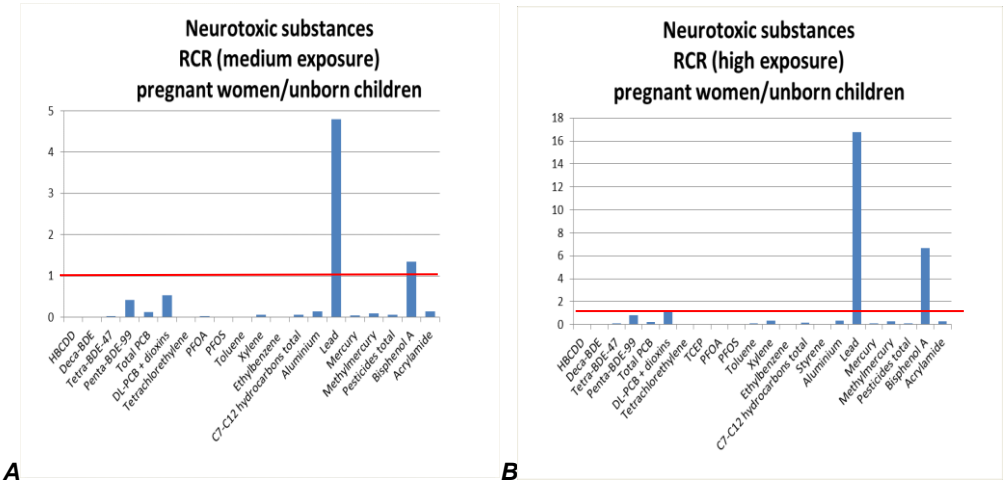
As appears from Figure 8.10 and Appendix 8G, it is the exposure to lead (RCR = 51) that plays a dominant role in this context. Besides lead, the following substances contribute the most to the overall RCR: brominated substances (penta-BDE-99; tetra-BDE-47; HBCDD), bisphenol A, dioxins and DL PCBs, mercury, aluminium, total PCB, acrylamide, mercury and PFOS and PFOA. In all, lead and these substances contribute with RCR = 60.6, and contributions from the other substances together represent a proportion of RCR = 0.5, of which 8 pesticides together result in RCR = 0.13.

High exposure

It appears that also here, lead (RCR = 231) plays a dominant role. Overall, the same above-mentioned substances contribute most to the total RCR. The total RCR for brominated substances (penta-BDE-99 and tetra-BDE-47), bisphenol A, dioxins and DL PCBs, mercury, aluminium, HBCDD, total PCB, acrylamide, mercury and PFOS and PFOA plus lead is 260.

8.3.3 Individual substances, pregnant women/ unborn children

Below in Figure 8.11, RCR values for the individual neurotoxic substances are shown in bar charts for medium and high exposure.



A ***B***

Figure 8.11 Pregnant women/ unborn children, RCR values for the individual neurotoxic substances at medium (A) and high (B) exposure.

Medium exposure

It appears that also for pregnant women/ unborn children exposure to lead (RCR = 4.8) plays a dominant role in the total RCR value of 7.9. For pregnant women/ unborn children can be seen that for the substances previously mentioned (brominated substances (penta-BDE-99 and tetra-BDE-47), bisphenol A, dioxins and DL PCBs, mercury, aluminium, HBCDD, total PCB, acrylamide, mercury and PFOS and PFOA plus lead), these contribute with a total RCR of 7.7 (With the four substances lead, penta-BDE-99, bisphenol A and dioxins and DL PCBs contributing with RCR = 7.1). Contributions from other substances make up the remaining part of RCR = 0.2, of which 8 pesticides together contribute with RCR = 0.06.

High exposure

It appears that exposure to lead (RCR = 16.8) also here plays a dominant role. Overall, the same substances as mentioned above contribute with an RCR of 26.8, where lead, penta-BDE-99, bisphenol A and dioxins and DL PCB in total contribute with RCR = 25.4. The other substances contribute with a total RCR of 0.8.

8.3.4 Special scenarios

The following are the RCR values for specific scenarios.

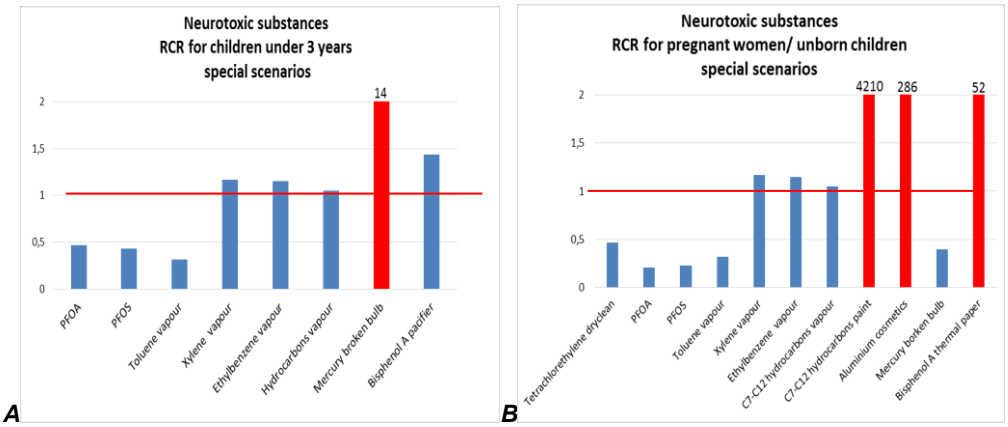


Figure 8.*12 RCR values for special scenarios for A: children under 3 years and B: pregnant women/ unborn children. The red bars indicate that the column goes beyond the diagram. The value is shown above the column.*

In connection with selected individual scenarios, the RCR value of 1 is exceeded for the following substances and scenarios for *children under 3 years*:

Mercury:	*RCR = 14; exposure associated with broken energy saving bulb*
Bisphenol-A:	*RCR = 1.4; exposure associated with use of pacifier*
C7-C12 –hydrocarbons:	*RCR = 1.05; vapours from petrol can outdoor, leaking into the home*
Ethylbenzene:	*RCR = 1.15; vapours from petrol can outdoor, leaking into the home*
Xylene:	*RCR = 1.17; vapours from petrol can outdoor, leaking into the home*

In connection with selected individual scenarios, the RCR value of 1 is exceeded for the following substances and scenarios for *pregnant women/ unborn children*:

Bisphenol-A:	*RCR = 52; exposure associated with contact with cash receipts*
C7-C12 –hydrocarbons:	*RCR = 4210; use scenario application of alkyd paint indoors*
C7-C12 –hydrocarbons:	*RCR = 1.05; vapours from petrol can outdoor, leaking into the home.*
Ethylbenzene:	*RCR = 1.15; vapours from petrol can outdoor, leaking into the home.*
Xylene:	*RCR = 1.17; vapours from petrol can outdoor, leaking into the home.*
Aluminium:	*RCR = 286; use of cosmetics containing aluminium*

It should be emphasised that the relevance of the calculated RCR values for each scenario will be discussed in more detail under the discussion of the individual substances, before any final decision can be made as to whether the scenarios pose a risk.

8.3.5 Biomonitoring data

RCRs from exposure estimates based on biomonitoring data are given in Table 8.7 for children under 3 years and in Table 8.8 for pregnant women/ unborn children. Also RCR values obtained from exposure estimates based on the traditional calculation method is given in order to compare the two sets of exposure estimations.

Table 8.7 Children under 3 years, RCR calculated from biomonitoring data and from traditional calculated exposure data.

Substance		Biomonitering				Modelled data	
	DNEL µg/kg/d	Medium exp. µg/kg/d	High exp. µg/kg/d	RCR Medium exp.	RCR High exp.	RCR Medium exp	RCR High exp.
Tetra-BDE-47	0.07	0.01	0.10	0.13	1.4	0.26	1.0
Penta-BDE-99	0.0017	0.003	0.04	1.8	25	4.1	15
PCB-7*	0.025**	1.0	2.7	40	109	0.25	0.77
PFOS	0.03	0.02	0.054	0.67	1.8	0.047	0.13
Bisphenol A	0.16	0.066	0.28	0.41	1.8	2.4	5.5
Acrylamide	3.40	0.54	1.9	0.16	0.56	0.41	0.71

**PCB biomonitoring in breast milk. Modelled PCB data do not comprise breast milk.*

***The DNEL value for PCB7 is estimated from DNEL for PCB total by using a correlation factor of 2, as this acc. to. (Danish EPA 2014) is the approximate ratio between total PCB and PCB7 in human tissue and foods.*

Table 8.8 Pregnant women/ unborn children. RCR calculated from biomonitoring data and from traditional calculated exposure data.

Substance		Biomonitoring				Modelled data	
	DNEL µg/kg/d	Medium exp. µg/kg/d	High exp. µg/kg/d	RCR medium exp.	RCR High exp.	RCR medium exp.	RCR High exp.
Bisphenol A	0.160	0.04	0.24	0.25	1.5	1.35	6.66

It is difficult to make a direct comparison of the RCR values based on biomonitoring data and the RCR values based on calculated exposure levels as the target groups in the biomonitoring studies do not necessarily reflect the target groups of this project, but often constitute a small subset of the population. Further, the biomonitoring studies may also have other objectives and are therefore, not directly targeted towards the type of exposure estimations specifically addressed in this project.

The discussion of the result of the biomonitoring data is included in the discussion for the individual substances/ substance groups below in Section 8.3.7.

8.3.6 Risk assessment in connection with analyses for bisphenol A in pizza boxes

In this project, analyses of pizza boxes were carried out for content of bisphenol A and phthalates. Levels of bisphenol A in pizza boxes were measured using 50 % ethanol extraction equal to the total content in the cardboard, because the cardboard structure was destroyed

during stay in the migration liquid. However, using an analytical method specifically for migration (sampling in Tenax powder) did not result in bisphenol A levels above the detection limit of the method. For an initial risk assessment the detection limit may therefore be used as a starting point for the exposure estimation. For children under 3 years and pregnant women/ unborn children, exposure levels of 2.4 µg/kg/d and 1 µg/kg/d were calculated, if bisphenol A migrates out of cardboard and into the pizza at a level corresponding to the detection limit in the migration test. As DNEL for bisphenol A for chronic neurotoxic effects is 0.16 µg/kg/d, it would thus in both cases lead to an RCR value exceeding 1.

However, since it is not known whether there is migration of bisphenol A at all, it cannot be concluded that there is a risk by eating pizza. It would require development of analytical methods with lower detection limit to make a more reliable assessment of the scenario.

8.3.7 Discussion of findings for the individual neurotoxic substances/ substance groups

In this section, data for the substances found to be of greatest importance (i.e. the highest RCR values) for chronic neurotoxic effects will be discussed with regard to the interpretation and uncertainties in connection with:

- *RCR values*
- *exposure sources and estimates*
- *hazard assessment and the DNEL value*
- *any exposure estimates based on biomonitoring data*

and also

- *lack of knowledge*
- *regulatory aspects*

In the discussion regarding exposure estimates and DNEL values reference is given to the information provided in Appendices 6a and 7a for the specific substances.

Lead

For children under 3 years, an RCR value for lead of 51 has been calculated at the medium exposure level. I.e. lead has primary responsibility for the overall RCR value of 61.1 when adding all RCR contributions for all the neurotoxic substances. For high exposure through foods and consumer products, an RCR value of 231 is achieved for lead.

This means that the exposure of children under 3 years is 51-231 times above the tolerable exposure level of 0.05 µg/kg/d indicated by EFSA (2010) and ECHA/ RAC (2014). By medium exposure, about 50 % of the exposure is considered to come from foods and drinking water while about 35 % is from dust and soil, and the remaining amount of approximately 15 % from lead containing articles/ products that may be subject to mouthing by children. At high exposure, mouthing of articles/ products may contribute to about 40 % of the total lead exposure.

Although there are uncertainties in these estimates, there is extensive data material behind the estimate of the lead content in the different sources/ products and exposure from these. The conclusions with regard to lead and its exposure estimates are considered reliable as they can be, from the measured content of the sources. The exposure estimates originate from expert groups under the European Food Safety Authority, EFSA and the European Chemicals Agency, ECHA. It may be anticipated, however, that mouthing of objects may contribute less in future due to more strict regulation regarding lead content in various articles.

There are no newer Danish biomonitoring studies examining lead in small children and women/ pregnant women. Such data would provide a better basis for a more accurate risk assessment based on the actual lead exposure to children under 3 years and pregnant women.

The tolerable exposure level for lead has by ECHA/ RAC been determined as a DMEL value (Derived minimal effect level) and not a DNEL value (derived no-effect level), as it was concluded that a lower level of exposure without harmful effects could not be determined. It was evaluated that an exposure of children to 0.5 µg/kg/d would results in a harmful impact on the central nervous system corresponding to a loss of one IQ point. The calculated exposures for children under 3 years are thus a factor of 5-23 above this level, and therefore it must be expected that the current lead exposure of children has harmful impact in terms of loss of IQ.

The use of lead and lead compounds is very strictly regulated in Denmark and in the EU in all administrative sectors, and it is therefore expected that the lead exposure will continue to decrease as seen for decades. Especially in Denmark, lead is subject to very restrictive regulated via the lead executive order prohibiting the import and sale of products with higher content than 100 mg lead/ kg (0.01 %) (some exemptions apply for specific purposes). Furthermore, EU limit values have been implemented for lead in the most relevant sources of food. In drinking water, an EU and Danish limit value of 10 µg/lead/l applies. A child under three years is estimated to drink 0.03 L/kg/d and 0.08 L/kg/d at average and high intake levels, respectively. This will contribute with 0.3 µg lead/kg/d and 0.8 µg lead/kg/d, which is 6 to 16 times above the tolerable level of exposure. In connection with a typical average content of about 0.9 µg Pb/L in drinking water, the child would be exposed to 0.027 µg Pb/kg/d and 0.072 µg Pb/kg/d for an average and high water intake, which is below and above, respectively, the tolerable level of exposure.

The reason for the high RCR values, however, is that the tolerable exposure level in the most recent expert assessments has been reduced from 3.6 µg/kg/d to 0.05 µg/kg/d (i.e. a reduction by a factor of 70) based on a new assessment method used by EFSA and ECHA/ RAC.

Therefore, there are good reasons to further reduce the use of lead and to monitor the levels in the environment and in food and consumer products.

Aluminium

For aluminium, the calculated RCR values for children under 3 years are 0.45 and 0.95 for medium and high exposure scenarios, respectively in relation to food consumption. For pregnant women/ unborn children, these RCR values are 0.14 and 0.32, respectively. For pregnant women/ unborn children an RCR of 286 is achieved by estimating a concrete scenario with high consumption of cosmetics.

For children under 3 years, the exposure is only from intake via foods, and the obtained RCR values are relatively close to 1 associated with high exposure. For pregnant women/ unborn children, exposure via foods constitutes around 1/3 of the level for children under 3 years.

However, women may be further exposed via the use of cosmetic products. SCCS (2014) refers to Norwegian exposure estimates for cosmetics (lipstick and anti-perspirant) that indicate an exposure of up to 86 µg/kg/d at high exposure (damaged skin). This corresponds to an RCR of 286. By medium exposure to cosmetics containing aluminium, the RCR value is 15 (intact skin). This indicates that in cases where pregnant women use cosmetics containing aluminium, there will be a risk for chronic neurotoxic effects for the fetus. It should be emphasised that the exposure assessment was based on a dermal absorption rate of 0.6 % for intact skin for a typical scenario, while the high exposure scenario was calculated with an absorption of 10.7 % in relation to damaged skin. SCCS, however, considered data on dermal absorption to be extremely uncertain and assessed that it was not possible to draw conclusions regarding internal dose by dermal application of cosmetics containing aluminium compounds.
The DNEL value for aluminium is estimated based on a 12-month developmental study in rats (SCCS 2014). SCCS also noted that an association has been found between exposure to aluminium and the development of several neuro-degenerative diseases in humans, but con-

sidered the data as insufficient for a causal relationship. The existing evidence from animal studies also have certain limitations, and therefore the DNEL value is considered to be associated with some uncertainty.

Overall, the assessment of aluminium is considered very uncertain, as there is a lack of knowledge regarding the bioavailability of aluminium in connection with intake from foods and not least in connection with dermal absorption from use of cosmetic products.

Bisphenol A

For children under 3 years and pregnant women/ unborn children, medium and high exposure result in RCR values ranging from 1.35 to 6.66, i.e. all above 1.
For children under 3 years, the contribution from foods is around 97 % while the remaining contribution comes from dust, toys and other consumer products (EFSA 2015). Also, the content of bisphenol A in pacifiers has previously been found to be a source.

For pregnant women/ unborn children, the food contribution is 36-71 % of the total exposure, where the remaining part of the exposure is from dust, cash receipts, cosmetics and other consumer products. Especially the content in cash receipts has raised concern, which has led to a ban for this use.

For children under 3 years, the RCR values based on biomonitoring data are lower than the RCR values calculated on the modelled data, cf. Table 8.5, where only RCR for the high exposure value exceeds 1 for the biomonitoring data. Biomonitoring data estimates are based on children between 6-11 years, as data are lacking for children under 3 years. However, the exposure of children under 3 years is considered to be higher, as the exposure via toys and dust can be expected to decrease with age.

For pregnant women/ unborn children, the RCR values based on biomonitoring data are lower than the RCR calculated on the modelled data, cf. Table 8.6, where only the RCR value of the high exposure exceeds 1 for biomonitoring data. Biomonitoring data are based on Danish women and are considered representative for pregnant women/ unborn children.

Overall, data regarding exposure to bisphenol A are considered reliable as data in 2015 have been assessed by expert groups under the European Food Safety Authority and the European Chemicals Agency.

The DNEL regarding neurotoxic effects has in 2015 been set to an oral dose of 0.16 µg/kg/d according to the Risk Assessment Committee under the European Chemicals Agency. This assessment is not consistent with the assessment by an expert group under EFSA who in 2015 evaluated the data on the neurotoxic effects to be too uncertain to form basis for derivation of a tolerable exposure level. However, EFSA, still considered neurotoxicity as part of an overall assessment of the uncertainties regarding other effects of bisphenol A than harmful effects on the kidneys that was considered the most critical effect. Thus, EFSA determined a provisional tolerable exposure level of 4 µg/kg/d from data on adverse effects on the kidneys and with an assessment factor based on the assessment of the uncertainties of other effects, including neurotoxic effects. If EFSA's tolerable level of exposure was used, the RCR values would thus be 1/25 of the calculated and give no cause for concern.

Regarding regulation of bisphenol A, migration limits have been set for food contact materials and toys and bisphenol is banned for use in cosmetics. By 2 January 2020 the substance may no longer be used for cash receipts. There are no data to evaluate neurotoxic properties for the possible alternative substances bisphenol F and bisphenol S.

Brominated substances ***(HBCDD; tetra-BDE-47 and penta-BDE-99)***
For the brominated substances, the following RCR values are obtained for children under 3 years for medium and high exposure scenarios, respectively:
RCR (HBCDD): 0.018 and 0.83
RCR (tetra-BDE-47): 0.26 and 1
RCR (penta-BDE-99): 4.1 and 15
For pregnant women/ unborn children, the highest RCR value was 0.82 in relation to high exposure to penta-BDE-99.

The calculated exposure estimates for children under 3 years regarding HBCDD are to a high degree dominated by exposure via dust. The data used for dust exposure may be considered very uncertain for Danish conditions, as the data is from relatively small foreign studies. If exposure is assessed based on content in foods alone, an RCR = 0.007 for the high exposure scenario for HBCDD can be achieved. There is no data on exposure to HBCDD from other sources. Thus, there is lack of knowledge about exposure from other sources, e.g. consumer products, and not least the indoor air dust, to more accurately assess the significance of HBCDD in relation to the risk of neurotoxic effects in children under 3 years.

For tetra-BDE-47 and penta-BDE-99, for children under 3 years and pregnant women/ unborn children, exposure estimates are based solely on the content in foods (EFSA 2011b) and no other sources are indicated for these substances. Even though data are limited, the uncertainties for these substances in relation to exposure are considered significantly less compared with the uncertainties regarding DNEL (see below).

EFSA's expert assessments provide the data basis for exposure and hazard assessments of all three substances (EFSA 2011a + b). For all three substances, EFSA evaluated the neurotoxic effects as being the most critical effects. This was based on observed changes in behavior in newborn mice in three mouse studies in which the mice were exposed once after birth. Although EFSA conducted risk assessment based on these experimental data, it was assessed that data were too uncertain to determine an actual tolerable exposure level.

The derived DNEL values for this project based on data reported in the EFSA's assessment should be regarded as rather uncertain, which has to be considered when assessing the importance of the RCR values for these substances.

Regarding biomonitoring data for children under 3 years, higher RCR values have been calculated using estimates based on biomonitoring data compared to RCR calculated using the modelled exposure data, cf. Table 8.1. Here it appears that RCR for the high exposure from the biomonitoring exceeds 1 for both tetra-BDE47 and penta-BDE-99. Biomonitoring data estimates are based on measurements made in breast milk and estimated intake by infants.

No relevant biomonitoring data were found with exposure estimates for pregnant women/ unborn children, although measurable levels of brominated flame-retardants in women are found in several Danish studies (see Appendix 6c).

Overall, it is evaluated that more robust data basis is required (both in terms of exposure and DNEL value) for the assessment of the significance of these three substances in relation to the risk of neurotoxic effects in children under 3 years and pregnant women/ unborn children. HBCDD is on the candidate list and the authorisation list in connection with the REACH regulation, while there is no specific regulation regarding tetra-BDE-47 and penta-BDE-99.

Dioxins and PCB

For children under 3 years, the RCR values for medium/ high exposure are 1.1 and 2.3, while the corresponding values for exposure of pregnant women/ unborn children are 0.5 and 1.2. For both medium and high exposure to dioxins and dioxin-like PCBs, almost 100 % of the exposure is from the intake of foods and, thus, all other sources are assessed to be of much less importance. The exposure estimates are considered highly valid based on monitoring data of foods in the EU and in Denmark (EFSA 2012 and DTU Food Institute).

In addition, there may be exposure to PCB from indoor air and dust in buildings where PCB-containing building materials (typically sealants) have been used. It has not been possible to calculate the RCR value for this contribution, as the PCB composition in air mainly comes from the most volatile PCB components, for which a DNEL value for neurotoxic effects cannot be readily stated.

Due to the content of dioxins and PCB in breast milk, however, very high RCR values are achieved for breastfeeding infants. German biomonitoring data from 2000-2003 indicate that the exposure through breast milk corresponds to an RCR value of 131 for dioxins and dioxin-like PCB. Biomonitoring data from Switzerland from 2004-2006 indicate total PCB content in breast milk, resulting in RCR values of 40 and 109, respectively, for medium and high exposure.

When calculating the RCR value for dioxins and dioxin-like PCB, the current tolerable exposure level of 2 pg TEQeqv/kg/d has been used. This value is derived considering neurotoxic effects as well as reproductive toxic effects by the Scientific Committee on Food (SCF 2001). When calculating the RCR value for total PCB, DNEL is determined from neurotoxic effects in a study in monkeys exposed to a PCB mixture corresponding to the composition in human breast milk (the study is described in Danish EPA 2014).

It can be seen that a significantly higher RCR value is achieved in connection with the breast-fed child compared to the non-breastfed child. However, there are significant advantages in breastfeeding children, which are considered to outweigh/ overshadow any increased risk of chemical exposure to PCB and dioxins in breast milk. In order to obtain more precise knowledge and balance of this aspect for Danish conditions, it would require measurements of PCBs and dioxins in breast milk of women in Denmark; as such data are not available at present.

Acrylamide

For acrylamide, the calculated RCRs for children under 3 years are 0.41 and 0.71 for medium and high exposure scenarios, respectively. For pregnant women/ unborn children the RCR values are 0.14 and 0.29, respectively.

All the exposure estimates for acrylamide are solely related to foods, as acrylamide is formed when baking/ roasting/ toasting a variety of foods (e.g. bread, potatoes, coffee). Other sources are assessed to be negligible. The exposure estimates are considered very reliable, as they have been obtained from relatively new and comprehensive measuring programs of foods in the EU and Denmark.

As the high exposure scenario for children under 3 years with an RCR value of 0.71 represents a 95-percentile level, it would be expected that some of the 5 % of children exposed to higher levels might exceed an RCR value of 1.

As the RCR values for pregnant women/ unborn children are lower than the RCR for children, and well below 1, acrylamide is not considered one of the most significant contributors to the risk of neurotoxic effects in unborn children.

The tolerable level of exposure or DNEL value for oral exposure of 3.4 µg/kg/d for neurotoxic effects, is established by EFSA (2015) from a relatively new (2012) chronic rat study, so the value is considered reliable. DNEL is based on peripheral nerve damage, so it is debatable whether it is fair to add the RCR value for acrylamide to the RCR value for other neurotoxic substances affecting the central nervous system.

It is seen from Table 8.1 that also the RCR values calculated from estimates based on biomonitoring data for children are below 1 for both medium and high exposure and these RCR values are in line with the RCR values based on EFSA's calculated exposure estimates.
No biomonitoring studies were found for women/ pregnant women.

Mercury, **inorganic**
For mercury, the calculated RCR values for children are 0.27, 0.44 and 14, for medium and high exposure and a single scenario with a broken energy-saving bulb, respectively. For pregnant women/ unborn children, these values are 0.04, 0.11 and 0.4.

All exposure estimates for medium and high exposure (95-percentile) are solely from food exposure. However, they are considered as valid estimates as data is from recent EU monitoring data on foods (EFSA 2012).

Although the RCR values are below 1, the values, in connection with an additive approach including other neurotoxic substances, are nonetheless significant background contributions, which can be significant particularly for children under 3 years.

An absolute worst-case scenario described by the Scientific Committee SCHER (2010) includes inhalation of mercury vapor from a broken energy-saving bulb. For this scenario where it is assumed that all mercury evaporates and that there is no form of ventilation of the room, an RCR of 14 can be achieved. SCHER (2010) assesses, however, that there is no risk of harmful effects by such an isolated and very short exposure represented by this scenario.

The tolerable exposure level (DNEL) for oral exposure is 0.7 µg/kg/d for neurotoxic effects. The value is established by EFSA (2012) from a study from 2011, which demonstrated behavioural effects and ear damage in newborn mice exposed in the embryonic and fetal periods and 3 weeks after birth. The DNEL derived from these data is considered to be well substantiated.

Besides the regulation of mercury in foods, cosmetics and toys, the Danish statutory order concerning mercury prohibits import and sale of mercury and mercury-containing compounds. Due to the strict regulation mercury exposure can be expected to continue to decline.

Methyl mercury
For methyl mercury, the calculated RCR values for children are 0.21 and 1.2, respectively, for medium and high exposures. For pregnant women/ unborn children, these values are 0.1 and 0.27.

Foods and especially fish products are sources of exposure to methyl mercury.
The exposure estimates for medium and high exposures (the latter as a 95-percentile value) are derived from monitoring of foods in the EU and must be considered reliable, although because of lacking Danish data, there is some uncertainty about exposure of Danish children under 2-3 years.

Because of an RCR value above 1 at high exposure, it must be expected that a smaller percentage of Danish children under 3 years is exposed to methyl mercury levels that may pose a risk of chronic neurotoxic effects.

Furthermore, there may be a significant single exposure to ethyl mercury (about 25 µg equal to about 2 µg/kg for a child of 2 years), as ethyl mercury is used as a preservative in some vaccines.

No exposure estimates were found based on biomonitoring data in the Danish studies, but mercury measurements made in hair from Danish women showed measurable levels in all participants of the study. Women with high intake of fish had higher levels of mercury in their hair (marker for exposure to methyl mercury) compared to women with a low intake of fish (Mørck et al. 2015a), which reinforces the fact that fish products are a significant source of exposure to methyl mercury.

Although the RCR values are below 1 for pregnant women/ unborn children, the values, in connection with an additive approach including other neurotoxic substances, may contribute to the risk of neurotoxic effects in unborn children, especially for mothers with a high consumption of fish.

Furthermore, there may be single exposure with the “sister” substance ethyl mercury because ethyl mercury is used as a preservative in some vaccines (approximately 25 µg/ dose).

The tolerable exposure level (DNEL) for methyl mercury for oral exposure is 0.19 µg/kg/d for neurotoxic effects. The value is established by EFSA (2012) based on data from population surveys, where population groups exposed to methyl mercury exhibited impaired performance in behavioural tests. This DNEL can be regarded as well substantiated.

C7-C12 hydrocarbons, ethylbenzene, xylene
For these substances, an RCR values above 1 are achieved for specific single scenarios. For children under 3 years, the following RCR values are achieved based on measurements in a children's room in connection with leakage of gasoline vapours from a tool shed, where lawn mower gasoline was kept: C7-C12 hydrocarbons: 1.05, Ethylbenzene: 17.01; Xylene: 1.15. Similar RCR values are achieved in cases where pregnant women are staying in the home. Although, there is generally relatively low RCR values for the substances in the indoor environment, the scenario with lawnmower gasoline (which may not be so rare) shows that specific (and unexpected) sources may cause significantly elevated indoor levels of these hydrocarbons

Additionally, for pregnant women/ unborn children an RCR value for C7-C12 hydrocarbons of 4210 can be calculated from a scenario where, contrary to all recommendations, painting with alkyd paint is done indoors in a small and poorly ventilated room. The scenario is from the Danish EPA LOUS report for white spirit, where this worst-case exposure for the use of alkyd paint indoors was derived from measured data. The scenario is based on older measurements with alkyd paint, and today alkyd paint is hardly used indoors. The scenario and the very high RCR value indicate, however, that even painting of smaller surfaces with alkyd paint indoors gives rise to RCR values exceeding 1.

The DNEL values for neurotoxic effects for the various hydrocarbons are derived based on extensive data material from experimental animal studies and from studies in the working environment, which have shown that neurotoxicity is the most critical effect in connection with prolonged exposure to the substances (Danish EPA 2016a). It should be emphasised that chronic effects of these substances, from exposure to gasoline or white spirit vapours, are the result of many years of exposure to the substances at levels far above the odour threshold, so single short-term exposure is unlikely to cause increased risk for chronic effects. Short-term, slightly elevated levels are more likely to cause odour nuisances, while highly elevated levels associated with painting may cause discomfort in the form of respiratory and eye irritation and transient neurotoxic effects such as headache and dizziness.

PFOS and PFOA

The sum of PFOS and PFOA results in an overall RCR value for children of 0.17 for medium exposure and 0.32 for high exposure, while the corresponding values for pregnant women/ unborn children is calculated to be 0.035 and 0.072.

EFSA (2013) indicates, however, a wide range for the exposure estimates, and using maximum concentrations found in foods, a worst case RCR of 0.90 can be calculated for children under 3 years and 0.43 for pregnant women/ unborn children for the sum of PFOA and PFOS. The exposure to PFOS (and PFOA) primarily originates from foods.

Data from a German biomonitoring study, in which PFOS in breast milk was studied, indicate that children who are breastfed in some cases would receive an exposure where the RCR value exceeds 1.

The DNEL of 0.03 µg/kg/d for PFOS and PFOA is based on data assessed by the US EPA (2016) concerning behavioural changes in a behavioural test with rat pups where the dams were dosed during gestation and during lactation.

8.3.8 Overall assessment of risk sources for neurotoxic effects

8.3.8.1 Most important substances

Children under 3 years

Table 8.9 lists the substances considered to have the greatest impact on the risk for chronic neurotoxic effects associated with exposure of children under 3 years. Furthermore, the background data for the assessments at the same time considered are the best documented when considering all the neurotoxic substances.

Table 8.9 Overview of chronic neurotoxic substances' contribution to RCR (medium exposure, high exposure) and sources to exposure for children under three years.

Neurotoxic substance	Sources	RCR Medium exposure	RCR High exposure
Lead	Foods, dust/ soil, articles	51.2	231
Bisphenol A	Foods, articles	2.42	5.49
Dioxins and dioxin-like PCB	Foods	1.05	2.30
Acrylamide	Foods	0.41	0.71
Mercury	Foods	0.27	0.44
Methyl mercury	Foods	0.21	1.21
RCR total for the above substances		*56*	-
PCB7	Breast milk breastfeeding	40	109
PFOS	Breast milk breastfeeding	0.67	1.8

For lead, which causes the highest risk for chronic neurotoxic effects, the exposure comes from foods, soil/ dust and lead-containing articles/ objects that may be subject to mouthing by children.
For all other substances, the vast majority of the exposure comes from food. For PCBs and dioxins, the most significant source is breast milk during the lactation period of the child. Individual data suggest that this may also be the case for PFOS.
As the background exposure via foods is of great importance for all substances, children will usually be exposed to several of these substances simultaneously, which support an additive approach of RCR values from for the individual substances contained in food. Addition of all the RCR values for simultaneous high exposure of all the substances is considered to be unrealistic.
The other 20 substances included in the assessment (including the brominated compounds, hydrocarbons and pesticides) must, based on the present analysis, be considered only to contribute marginally to the increased risk for chronic neurotoxic effects compared to the substances listed above.

Pregnant women/ unborn children
Table 8.10 lists the substances considered to have the greatest impact on the risk for chronic neurotoxic effects associated with exposure of pregnant women/ unborn children. Furthermore, the background data for the assessments are at the same time considered the best documented when considering all the neurotoxic substances.

Table 8.10 Overview of chronic neurotoxic substances' contribution to RCR (medium exposure, high exposure) and sources to exposure of pregnant women/ unborn children.

Neurotoxic substance	Sources	RCR Medium exposure	RCR High exposure
Lead	Foods (incl. drinks)	4.8	16.8
Bisphenol A	Foods, articles	1.35	6.66
Dioxins and dioxin-like PCB	Foods	0.53	1.15
Penta-BDE-99	Foods	0.41	0.82
Mercury	Foods	0.03	0.11
Methyl mercury	Foods	0.1	0.27
RCR total		***7.3***	**-**

For lead, bisphenol A, dioxins and dioxin-like PCB, and methyl mercury, it apply that the vast majority of the exposure of pregnant women/ unborn children comes from foods. For bisphenol A, there is also a significant contribution from articles, including cash receipts (however, the latter will be prohibited from 2020).

As the background exposure of pregnant women/ unborn children via foods is of great importance for all the substances, unborn children (via the pregnant women) will be exposed to several of these substances simultaneously every day, which supports that the RCR values for medium exposure of the chronic neurotoxic substances contained in food may be added. However, addition of all the RCR values for simultaneous high exposure of all substances is not considered unrealistic.

There will continuously be a need to assess whether there may be additional unintended exposure to the substances through consumer products, as any new sources could increase the RCR values further.

8.3.8.2 Knowledge base

The other 20 substances included in the assessment (e.g. the fluorinated compounds and pesticides) must, based on the present analysis, be considered only to contribute marginally to the increased risk of neurotoxic effects compared to the substances listed above. However, it should be noted that many of these substances are less well-studied substances and that increased use and new knowledge about the neurotoxic effects typically will result in lower DNEL values and thus increase the RCR values for the substances.

The above overview of the substances that contribute the most to the overall risk of neurotoxic effects shows that for several substances, knowledge of human exposure is lacking, and that increased knowledge on the toxic effects of the substances could reduce the uncertainty in the assessment. It is estimated that especially for the following substances, the best documentation is seen regarding knowledge about effects and levels of exposure: lead, dioxins and PCBs, bisphenol A.

However, for the substances with the greatest impact on the neurotoxic risk, i.e. lead, dioxins and PCBs, it may be relevant to obtain more precise knowledge about risk, because for these substances it is possible through biomonitoring data to achieve a more accurate description of the exposure. Especially biomonitoring data on lead in the blood of pregnant women (and possibly children under 3 years) and on the levels of dioxins and PCBs in breast milk would be helpful for more precise risk and impact assessment.

8.3.8.3 Regulation

Despite strict regulation for many of the substances continued exposure via e.g. food is still seen because of persistence/ accumulation in the environment, including pollution of soil. It can thus be difficult for consumers to avoid exposure to lead, dioxins and PCBs, for example. For bisphenol A that is not a persistent substance that accumulates, the exposure is more dependent on the actual uses of the substance, where regulation of the substance (e.g. food contact materials and articles e.g. toys for toddlers) will result in more rapid reductions of the exposure.

9. Discussion and conclusion

9.1 Discussion

This project presents an evaluation of the cumulated exposure of children under 3 years and pregnant women/ unborn children to a variety of endocrine disrupting (and suspected endocrine disrupting) and chronic neurotoxic substances.
The selection of endocrine disruptors (and suspected endocrine disrupting) and known chronic neurotoxic substances is based on knowledge gathered in by the Danish Environmental Protection Agency as well as knowledge from the scientific literature. The selection phase included an initial qualitative estimate of whether consumer exposure to the designated target groups was realistic. In order to conduct a risk assessment of the substances, it was necessary to focus on substances with data regarding exposure estimates for the target groups and with sufficient data on the toxicology of the substances to estimate a tolerable human exposure value (derived no effect level, DNEL) for endocrine disrupting and chronic neurotoxic effects, respectively.

Exposure
It was important for the project to achieve as updated and valid exposure data as possible in order to get a picture of the exposure of the target groups. The available exposure data were as far as possible divided into the following different sources of exposure:

- foods and drinking water
- indoor environment (dust, vapours) + outdoor environment (soil)
- cosmetics
- consumer products (articles, toys, chemical products, etc.)

In general, data for exposure via indoor environment, outdoor environment and consumer products are far from complete and also difficult to assess and as this project has shown often food exposure is best described and also constitutes the most significant source of exposure for most of the selected substances for which exposure data were found. However, it is not certain that this truly reflects the sources of human exposure to these substances. For the indoor environment and the outdoor environment, there is rarely as systematic analyses of exposure as for foods. Apart from a few substances, for which there are many data for content in the indoor environment (e.g. lead and phthalates) and content in soil (e.g. lead), data are often very scattered and it is also difficult to assess how representative these data are. Therefore, estimates of the indoor/ outdoor environment should be taken with some caution, e.g. when it comes to the contributions that in this report are assessed for e.g. brominated, chlorinated and perfluorinated substances.

For cosmetics, just as for foods, it applies that when used you are certainly exposed to the components herein. Knowledge of content in a cosmetic product and knowledge of average typical and high consumption would thus give a fairly accurate indication of the exposure of the individual consumer. The degree of public exposure will to a greater extent than the food exposure be determined by preferences for use, as the use of cosmetics varies much in the population. The exposure estimates in this report are based largely on assumptions, as exposure estimation for consumer products is substantially less standardised than for e.g. foods and cosmetics.

Hazard assessment

In this project, hazard assessments of the selected suspected endocrine disrupting and neurotoxic substances were carried out. It is essential to gather knowledge of dose-effect relationships for neurotoxicity and/ or endocrine disrupting effects of the substances, in order to derive a tolerable human exposure level (DNEL) based on a NOAEL, a LOAEL, or a benchmark dose and by assessment factors in accordance with the guidelines for the use of these. As for exposure estimation, uncertainties and limitations are associated when determining DNEL values. For endocrine disruptors, all DNELs were determined based on animal studies. For chronic neurotoxic substances, the starting points for DNEL calculation were very different. In one case, DNEL was determined based on only one study on newborn mice. In another case, IQ testing of thousands of children was used for DNEL derivation.

It should be noted that the terms "suspected endocrine disrupting" and "endocrine disrupting" substances reflect the degree of evidence for endocrine disrupting effects of a substance. The Danish proposal to criteria for the identification of endocrine disrupting potential is used in this project (Danish EPA 2011a). In the project, the term "endocrine disruptors" is used for the total group of substances that are either "suspected endocrine disrupting" or "endocrine disrupting" according to these criteria.
For endocrine disruptors, it there is an on-going discussion, whether a lower limit for the effects of endocrine disruptors can be determined with reasonable certainty (whether there is a threshold value for the effects) and thus, whether robust tolerable exposure levels (DNELs) can be derived. Since no alternative method has been developed yet to assess the risk of exposure to endocrine disruptors, a traditional risk assessment approach has been used here as described below. An advantage of this approach is that the risk of the combined exposure to multiple substances with the same modes of action can be calculated. If in future an agreement can be reached on an alternative method to assess the risk of endocrine disruptors, the calculations in this report should be reviewed accordingly. Such alternative risk assessment method is expected to result in lower DNEL values and thus higher calculated risk.

Risk assessment

In the project, a risk assessment for the overall exposure was carried out and the most important substances were identified. RCR-values (ratio between exposure estimate and DNEL) for the individual substances were added to illustrate the risk by simultaneous exposure to several substances having the same type of effects or mode of action. Simultaneous exposure to several chemical substances will typically occur for substance exposure through food content or content in drinking water and soil/ dust where several substances may occur simultaneously, just as you can be exposed to substances from various exposure sources simultaneously. Such addition of RCR alues for several substances was performed for both medium exposures and high exposures. The reliability of this addition approach is considered highest by addition of the RCR values for the medium exposures, as it seems unlikely that children or pregnant women should be simultaneously exposed to all substances at high exposure.

For **endocrine disruptors** (and suspected endocrine disruptors) the project found that intake of paracetamol at critical periods during the early development may result in risk for antiandrogenic effects, and the RCR values for paracetamol exceed the RCR values for the other substances.

This is because the risk assessment in this report is made according to the principles of environmental or food related substances, where an uncertainty factor of 100 is used and the risk assessment is based on high doses of medication. It has not been possible to estimate the use of Paracetamol among pregnant women and children under 3 years, as this product is sold as an over the counter pharmaceutical product.

Although it must be assumed that a small part of these groups uses paracetamol during a critical period of the fetal/ child development and that the duration of administration will reflect the recommendations from authorities. Consumers can control the therapeutic intake of paracetamol to a larger extent than other substances in this report, and in a risk assessment of medicinal products, the benefits should further be taken into account (see discussion in Section 8.2.9).

In Europe, the suspected hormone disrupting (antiandrogenic) effects of paracetamol have been discussed at several occasions. The Danish Medicines Agency reports that at present and based on the available data there is not sufficient evidence for an association between paracetamol and antiandrogenic effects. Both the experimental animal studies as well as epidemiological studies indicating such an association were considered too weak for concluding a causal relationship. The Danish Medicines Agency emphasises that when analgesics are needed then paracetamol is still recommended compared to other non-prescribed analgesics, as paracetamol is considered the least harmful for unborn children. Thus, it is important not to substitute paracetamol with other types of analgesics, e.g. ibuprofen, as this type of medicine is considered to have a greater toxic effect on the unborn child than paracetamol.

Also, it is recommended that paracetamol should only be used when there is a medical need and at lowest dose levels and for shortest duration, which is the general recommendation for all types of medical products used during pregnancy.

PCBs and dioxins contribute significantly with high RCR values. For children, intake of PCBs and dioxins in foods may alone exceed the tolerable exposure levels and thereby cause concern. Exposure via the indoor environment may also contribute, and here PCBs in dust are seen to contribute significantly.

The relatively high RCR values by exposure to certain phthalates (*DEHP, DBP, DIBP*) in foods, indoor environment and consumer products contribute significantly to the overall risk for antiandrogenic effects. As there is good agreement between the modelled exposure data and the estimates based on biomonitoring data, it is likely that a proportion of children and pregnant women/ unborn children are exposed to levels that give rise to concern in the overall risk assessment for antiandrogenic substances.

Bisphenol A from foods and consumer products contribute significantly to the total RCR values, and particularly by using the alternative, low DNEL (DTU 2015), bisphenol A exposure in itself can be of concern for estrogenic effects. The RCR values based on biomonitoring data are lower than the RCR values based on the modelled exposures.

BHA and BHT in foods is seen to contribute significantly to the total RCR, and in the scenario with high intakes, these substances alone can be of concern for thyroid hormone disrupting effects. There may also be a significant contribution from BHT in cosmetics, as in this project content of BHT was measured in a number of creams (BHA only in one single body oil). How-

ever, there is considerable uncertainty associated with the exposure calculations for BHT in cosmetics, given the lack of knowledge regarding absorption and metabolism in the body by dermal exposure.

For *butyl and propyl paraben and OMC* high RCR values may be of concern for persons using products with high contents of these substances. It should be noted that these figures are based on exposure scenarios with high consumption of cosmetic products with high contents of these substances. It is not clear whether these substances are typically used in the maximum allowable concentrations, and it should be noted that a lower real content will result in lower RCR values. It must be assumed that a minor part of the Danish children/ unborn children is exposed to such high exposures that may be of concern. This conclusion is supported by the fact that the RCR values based on biomonitoring data are lower than the RCR values based on the modelled exposures.

For **neurotoxic substances,** it can be seen that exposure to lead causes by far the highest risk for chronic neurotoxic effects among all the studied neurotoxic substances. Exposure to lead can be divided on the sources: foods + drinking water, soil/ dust and lead containing articles/ products that may be subject to mouthing by children. In foods, particularly drinks, but also fruit, vegetables and cereals represent the largest contribution to the exposure. Adverse effects from lead exposure is documented from several well-conducted epidemiological studies from US in which correlations were found between lead exposure during the embryonic stage and first years of life and reduced IQ. Thus, based on the findings on current exposure in this project it seems relevant to continuously follow the development of the presence of lead in foods and in articles. Measurement of lead content in the blood of children and pregnant women could give a more accurate picture of the actual exposure to lead and thus the risk for neurotoxic effects.

Also, exposure to dioxins and PCBs through foods and breast milk raises concern for chronic neurotoxic effects, where especially children under 3 years who are breastfed can achieve significantly elevated RCR values as a result of exposure through the breast milk. However, there are significant advantages in the child being breastfed, which are considered to outweigh/ overshadow any increased risk of chemical exposure to PCBs and dioxins in breast milk. To achieve a more precise knowledge and balance of this aspect for Danish conditions, this would require measurements of PCBs and dioxins in breast milk from Danish women as such data are not present. Data are considered too limited to assess any risk of neurotoxic effects due to PCBs in the indoor environment as a result of past use of PCB-containing building materials. Here, the exposure is dominated by the lower and most volatile PCBs, for which sufficient data have not been found regarding neurotoxic effects and thus, no DNEL can be derived for these PCBs and form a basis for a risk assessment.

For *mercury and methyl mercury,* exposure through foods (methyl mercury mainly from fish) gives a contribution that should count when looking at the overall exposure to neurotoxic substances. For children under 3 years, exposure may exceed the tolerable exposure level. A special contribution with mercury can occur in connection with broken energy-saving bulbs containing mercury. However, such exposure can be avoided if residues from the broken bulb are carefully removed and a thorough ventilation of the home is ensured.

Finally, increased risk of neurotoxic effects is estimated for exposure to *bisphenol A*. Here, it is primarily the exposure through foods, but there may also be exposure from the indoor environment and articles. Especially exposure through cash receipts may in special cases cause a large exceeding of the tolerable exposure level for pregnant women. For children under 3 years a potential content in pacifiers may cause an increased risk. The assessment of bisphenol A is uncertain, especially as there is disagreement between the EU expert committees (EFSA and the RAC Committee in ECHA) as to whether the data on neurotoxic effects are sufficient to justify a risk assessment for these effects.

Also, this project identified a number of other neurotoxic substances (e.g. some brominated and chlorinated flame-retardants, PFOA and PFOS, aluminium, and organic solvents and some pesticides). The exposure to many of these substances is very difficult to assess and quantify, but each small exposure could - although to a lesser extent than the above mentioned substances - make a contribution to the overall risk for neurotoxic effects.

Finally, it has not been possible in this project to include possible effects from a number of other potentially neurotoxic impacts, such as exposure to particles (ambient air), inorganic fluoride (drinking water and toothpaste), arsenic (drinking water and foods) and alcohol intake.

9.2 Conclusions

Despite uncertainties regarding the selection of substances, exposure assessment and determination of tolerable levels of exposure for endocrine disruptors and chronic neurotoxic substances, the results of this are considered to give indications of which substances that, based on present knowledge, are considered as the most critical ones in terms of increased risk for endocrine disrupting and neurotoxic effects in children under 3 years or in pregnant women/ unborn children. It is also clear that for a number of substances, it is not possible to assess the risk, given the lack of knowledge on human exposure and/ or on dose-response for adverse health effects.

Among the evaluated substances, the most significant endocrine disruptors to which children under 3 years and pregnant women/ unborn children may be exposed are *dioxins/ PCBs, phthalates (DEHP, DBP, DiBP), bisphenol A, BHA and BHT*. The exposure mainly comes from foods and, thus, is very likely to be recurring. For p*ropyl and butyl paraben and OMC*, there may be cause for concern regarding exposure from cosmetics for individuals exposed to large quantities of products with high contents of these substances in a sensitive period of development, as this may cause risk of endocrine disrupting effects.
The medicinal product *paracetamol* contributes with by far the highest RCR values, but it should be noted that the risk assessment has been carried out using the same principles as for environment or food related substances, in order to relate the risk for endocrine disrupting effects for all chemicals and all sources in the project. Risk assessment of medicinal products will generally be different from the risk assessment of chemicals from foods, cosmetics, indoor environment and consumer products, as medicinal products may have acceptable side effects and as the assessment primarily is based on human data.

The Danish Medicines Agency points out that the European Medicines Agency (EMA) has repeatedly assessed the available data and studies in humans and animals, and did not find sufficient evidence for a relationship between paracetamol and anti-androgenic effects. Therefore, the Danish Medicines Agency still recommends paracetamol as first-line treatment of pain for pregnant women and children, as paracetamol is considered less harmful for unborn children compared to other analgesics, e.g. ibuprofen. Also, it is recommended that paracetamol should only be used when there is a medical need and at lowest dose levels and for shortest duration, which is the general recommendation for all types of medical products used during pregnancy.

It is currently being discussed whether a lower limit for the effects of endocrine disruptors can be determined with reasonable certainty, and whether an alternative method of risk assessment should be used instead of the traditional one, where there is assumed to be a lower exposure threshold for the effect of a substance. In this project, it is decided to use the traditional risk assessment method and to determine DNEL values on this basis. If in future, agreement can be reached on another method to risk assess endocrine disrupting effects, it may be necessary to reassess the values accordingly. Such alternative risk assessment method is expected to result in lower DNEL values and thus higher calculated risk.

Concerning the neurotoxic assessment, the most significant *chronic neurotoxic substances* to which children under 3 years and pregnant women/ unborn children may be exposed are *lead, dioxins/ PCBs, mercury/ methyl mercury, bisphenol A and acrylamide*. Here, lead constitutes by far the highest risk of chronic neurotoxic effects. For all of the mentioned substances, exposure through food is the most significant source. Significant exposure to lead also occurs through drinking water, soil and metal objects (such as jewelry and other consumer articles) that can be mouthed by small children. Strict regulatory measures, however, may reduce lead exposure further in the coming years. It should be mentioned that breast milk is considered a major source of dioxin/ PCB exposure.

The above conclusions are based on a screening of the substances considered relevant for the exposure of children under 3 years and pregnant women/ unborn children to endocrine disrupting and chronic neurotoxic substances. For more than 60 substances, references have been collected regarding exposure and knowledge of the hazards of the substances and tolerable exposure levels. The results of the risk assessments are evaluated to have led to identification of the most critical substances. For some areas with identified risk, there may be a need for further analysis of this risk. This applies to children’s and pregnant women's exposure to lead, where any biomonitoring data would provide a better picture of the risk for neurotoxic effects in children, as this risk in this project is found to be very high. Similarly, breast milk analyses for PCB and dioxin could give a better picture of the impact of the exposure of infants through breast milk.

It is generally seen that it is difficult to obtain an accurate assessment of exposure via indoor environment and consumer products/ articles, as representative knowledge on public exposure via these sources is very incomplete.

Finally, it applies for exposure of pregnant women/ women of childbearing age that this project only focuses on the exposure as a consumer in connection with foods, cosmetics and consumer products. Women of childbearing age/ pregnant women may also be exposed to endocrine disrupting/ neurotoxic substances through other sources, e.g. in connection with exposure in the working environment, consumption of alcohol or smoking, or in connection with medicinal products.

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Appendix 1

Danish EPA list (2016) of endocrine disrupting chemicals and suspected endocrine

Bilag A – Bruttoliste over hormonforstyrrende og mistænkt hormonforstyrrende stoffer

Stofnavn	CAS nr.	EU-lister	REACH registrering	Kosmetik regulering	Fødevarekontaktmaterialer	
					EU Plast regler	CH Trykfarve regler
Ftalater						
DEHP (di-ethyl-hexyl-ftalat)	117-81-7	EU COM cat 1 SVHC ED ENV+Repr 1B SIN	10.000-100.000 t/år	Forbudt	Max 0,5% eller 1,5 mg/kg fødevare	Max 1,5 mg/kg fødevare
DiNP (di-iso-nonyl-ftalat)	28553-12-0	EU COM cat 2 SIN	100 000 - 1 000 000 t/år	Ureguleret Ikke i cosing	Max 0,1% eller 9 mg/kg (sum af DiDP og DiNP)	Max 9 mg/kg fødevare
DBP (di-butyl-ftalat)	84-74-2	EU COM cat 1 SVHC Repr 1B SIN	1000-10.000 t/år	Forbudt	Max 0,05% eller 0,3 mg/kg fødevare	Max 0,3 mg/kg fødevare
DiBP (di-iso-butyl-ftalat)	84-69-5	EU COM cat 2 SVHC Repr 1B SIN	1-10 t/år	Forbudt	Ikke tilladt	Max 0,01 mg/kg fødevare
BBP (butyl-benzyl-ftalat)	85-68-7	EU COM cat 1 SVHC Repr 1B SIN	1000-10.000 t/år	Forbudt	Max 0,1% eller 30 mg/kg fødevare	Max 30 mg/kg fødevare
DPP (dipentyl ftalat)	131-18-0	EU COM-cat 1SVHC	Præregistreret	Forbudt	Ikke tilladt	Ikke tilladt

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
		Repr 1B SIN				
DnHP (di-n-hexyl ftalat)	84-75-3	EU COM cat 2 SVHC Repr 1B SIN	Præregistreret	Forbudt	Ikke tilladt	Ikke tilladt
DnOP (Di-n-octyl ftalat)	117-84-0	SIN	Præregistreret	Ureguleret Ikke i cosing	Ikke tilladt	Max 0,01 mg/kg fødevare
DCHP (Dicyclohexyl ftalat)	84-61-7	EU COM cat 1 SIN	100-1000 t/år	Ureguleret Ikke i cosing	Ikke tilladt	Max 6 mg/kg fødevare
DEP (Diethyl ftalat)	84-66-2	EU COM cat 1 SIN CoRAP	1000-10000 t/år	Ureguleret, cosing (denaturant, hairconditioning, masking, solvent)	Ikke tilladt	Max 0,01 mg/kg fødevare
DPHP (Bis(2-propylheptyl) ftalat)	53306-54-0	CoRAP	100.000-1.000.000 t/år	Ureguleret Ikke i cosing	Ikke tilladt	Max 0,01 mg/kg fødevare
1,2-Benzenedicarboxylic acid, di-C6-10-alkyl esters	68515-51-5	SVHC Repr 1B SIN	100-1000 t/år	Forbudt	Ikke tilladt	Max 0,01 mg/kg fødevare
DIDP (1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich)	68515-49-1	SIN	100 000 - 1 000 000 t/a	Ureguleret Ikke i cosing	Max 0,1% eller 9 mg/kg fødevare (sum af DiDP og DiNP)	Max 9 mg/kg fødevare
Perfluorerede stoffer						
Perfluorododecanoic acid	307-55-1				Ikke på	Ikke tilladt

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
(PFdoDA)					positive liste	
Perfluoroundecanoic acid (PFunDA)	2058-94-8	SVHC vPvB			Ikke på positive liste	Ikke tilladt
Perfluorodecanoic acid (PFDA)	335-76-2				Ikke på positive liste	Ikke tilladt
Perfluorononanoic acid (PFNA)	375-95-1	SVHC Repr. 1B & PBT			Ikke på positive liste	Ikke tilladt
Perfluorooctanoic acid (PFOA)	335-67-1	SVHC Repr. 1B & PBT	Restriktion på vej		Ikke på positive liste	Ikke tilladt
Perfluoroheptanoic acid (PFHpA)	375-85-9				Ikke på positive liste	Ikke tilladt
Perfluorohexanoic acid (PFHxA)	307-24-4				Ikke på positive liste	Ikke tilladt
Perfluoropentanoic acid (PFPeA)	2706-90-3				Ikke på positive liste	Ikke tilladt
Perfluorobutanoic acid (PFBA)	375-22-4				Ikke på positive liste	Ikke tilladt

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
Perfluorooctane sulfonat (PFOS)	1763-23-1	POP Forordninigen Repr. 1B			Ikke på positive liste	Ikke tilladt
Perfluorohexane sulfonat (PFHxS)	355-46-4				Ikke på positive liste	Ikke tilladt
Perfluorobutane sulfonat (PFBS)	375-73-5				Ikke på positive liste	Max 0,01 mg/kg fødevare
8:2 Fluorotelomer alcohol (8:2 FTOH)	678-39-7		Restriktion på vej		Ikke på positive liste	Ikke tilladt
6:2 Fluorotelomer alcohol (6:2 FTOH)	647-42-7				Ikke på positive liste	Ikke tilladt
4:2 Fluorotelomer alcohol (4:2 FTOH)	2043-47-2				Ikke på positive liste	Ikke tilladt
10:2 Fluorotelomer phosphate triester (10:2 triPAPs)						
8:2 Fluorotelomer phosphate triester (8:2 triPAPs)			Restriktion på vej			
6:2 Fluorotelomer phosphate triester						

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
(6:2 triPAPs)						
4:2 Fluorotelomer phosphate triester (4:2 triPAPs)						
10:2 Fluorotelomer phosphate diester (10:2 diPAPs)						
8:2 Fluorotelomer phosphate diester (8:2 diPAPs)			Restriktion på vej			
6:2 Fluorotelomer phosphate diester (6:2 diPAPs)						
4:2 Fluorotelomer phosphate diester (4:2 diPAPs)						
10:2 Fluorotelomer phosphate monoester (10:2 monoPAPs)						
8:2 Fluorotelomer phosphate monoester (8:2 monoPAPs)			Restriktion på vej			
6:2 Fluorotelomer phosphate monoester (6:2 monoPAPs)						
4:2 Fluorotelomer phosphate monoester (4:2 monoPAPs)						
Bisphenoler						
Bisphenol A	80-05-7	EU COM cat 1 CoRAP SIN	1.000.000-10.000.000 t/år	Forbudt	Max 0,6 mg/kg fødevare	Max 0,6 mg/kg Fødevare
Bisphenol S	80-09-1	SIN CoRAP	1000-10.000 t/år	Ureguleret Ikke i cosing	Max 0,05 mg/kg fødevare	Ikke tilladt
Bisphenol M	13595-25-0	CoRAP	>1 t/år	Forbudt	Ikke tilladt	Ikke tilladt
Bisphenol F	620-92-8	SIN	Præregistreret	Ureguleret Ikke i cosing	Ikke tilladt	Max 0,01 mg/kg fødevare
UV-filtre						
Octyl methoxycinnamat, 2-ethylhexyl-4-methoxycinnamat (OMC)	5466-77-3	EU COM cat 1 CoRAP SIN	Præregistreret	Reguleret som UV-filter	Ikke tilladt	Max 0,01 mg/kg fødevare
3-Benzyliden camphor (3-BC)	15087-24-8	EU COM cat 1 SIN	Præregistreret	Forbudt	Ikke tilladt	Ikke tilladt
4-Methylbenzyliden camphor (4-MBC)	36861-47-9	EU COM-cat 1 SIN	Præregistreret	Reguleret som UV-filter	Ikke tilladt	Ikke tilladt
Benzophenon (BP)	119-61-9	EU COM-cat 3b CoRAP SIN	1000-10000 t/år	Ureguleret, cosing (Masking, UV-absorber)	Max 0,6 mg/kg fødevare	Max 0,6 mg/kg fødevare (sumgrænse)
Benzophenon-1 (BP-1)	131-56-6	EU COM cat 1 SIN	0-10 t/år	Ureguleret, cosing (UV-absorber)	Max 6 mg/kg fødevare	Max 6 mg/kg fødevare (sumgrænse)

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
					(sumgrænse)	
Benzophenon-2 (BP-2)	131-55-5	EU COM cat 1 SIN	Præregistreret	Ureguleret, cosing (Masking, UV-absorber)	Ikke tilladt	Max 0,01 mg/kg fødevare
Benzophenone 3 (BP-3)	131-57-7	EU COM cat 2 CoRAP SIN	100-1000 t/år	Reguleret som UV-filter	Max 6 mg/kg fødevare (sumgrænse)	Max 6 mg/kg fødevare (sumgrænse)
Benzophenon-12 (BP-12)	1843-05-6	CoRAP	100-1000 t/år	Ureguleret, cosing (UV-absorber)	Max 6 mg/kg fødevare (sumgrænse)	Max 6 mg/kg fødevare (sumgrænse)
Hydroxycinnamic acid	7400-08-0	EU COM cat 1	Præregistreret	Ureguleret, cosing (skinconditioning)	Ikke tilladt	Ikke tilladt
Octocrylen	6197-30-4	CoRAP	1000-10.000 t/år	Reguleret som UV-filter	Max 0,05 mg/kg fødevare	Max 0,05 mg/kg fødevare
Isoamyl-p-methoxycinnamat	71617-10-2	CoRAP	100-1000 t/år	Reguleret som UV-filter	Ikke tilladt	Ikke tilladt
Andre stoffer						
Dioxiner og sioxinlignende PCB'er						
Nonylphenol	25154-52-3	EU COM Cat 1		Forbudt	Ikke på	Max 0,01 mg/kg fødevare

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
		SVHC- ED ENV			positivliste	
TBBPA (tetrabromobisphenol A)	79-94-7	CoRAP SIN	1000-10.000 t/år	Ureguleret Ikke i cosing	Ikke på positivliste	Ikke tilladt
BEH-TEBP/BEHTBP (Bis(2-ethylhexyl) tetrabromophthalate)	26040-51-7	CoRAP SIN[c]	100-1000 t/år		Ikke på positivliste	Ikke tilladt
TBBPA oligomer (2,2',6,6'-Tetrabromo-4,4'-isopropylidenediphenol, oligomeric reaction products with Propylene oxide and n-butyl glycidyl ether)	UVCB	CoRAP (ED-concern)				
HBCDD (hexabromocyclododekan)	25637-99-4	Kandidatlisten (PBT) og Miljø-projekt 1823, 2016. (ED-concern)			Ikke på positivliste	Ikke tilladt
Deca-BDE (decabromineret diphenyl ether)	1163-19-5	Miljø-projekt 1823, 2016. (ED-concern)			Ikke på positivliste	Max 0,01 mg/kg fødevare
Octamethylcyclotetrasiloxan (D4)	556-67-2/293-51-6	EU COM Cat 1 SIN	100.000-1.000.000 t/år	Ureguleret, cosing (Emollient, hair- and skin conditioning, solvent)	Ikke på positivliste	Max 0,01 mg/kg fødevare
Decamethylcyclopentasiloxan (D5)	541-02-6		10.000-100.000 t/år	Ureguleret, cosing (Emollient, hair- and skin	Ikke på positivliste	Max 0,01 mg/kg fødevare

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
				conditioning, solvent)		
Propylparaben	94-13-3	EU COM Cat 1 SIN CoRAP	100-1000 t/år	Reguleret som konserveringsmiddel	Tilladt som additiv	Tilladt som additiv
Butylparaben	94-26-8	EU COM Cat 1 SIN	Præregistreret	Reguleret som konserveringsmiddel	Ikke på positivliste	Max 0,01 mg/kg fødevare
Isobutylparaben	4247-02-3			Forbudt	Ikke på positivliste	Ikke tilladt
Triclosan	3380-34-5	CoRAP SIN	Præregistreret	Reguleret som konserveringsmiddel	Ikke på positivliste	Ikke tilladt
Resorcinol	108-46-3	EU COM Cat 1 SIN CoRAP	10.000-100.000 t/år	Reguleret som hårfarve på bilag III (masking)	Max 2,4 mg/kg fødevare	Max 2,4 mg/kg fødevare
Butylated hydroxyanisol (BHA)	25013-16-5 / 88-32-4 / 121-00-6	EU COM Cat 1 SIN CoRAP	100-1000 t/år	Ureguleret, cosing (Masking, antioxidant)	Max 30 mg/kg fødevare	Max 30 mg/kg fødevare
2,6-di-tert-butyl-p-pcreosol (BHT)	128-37-0	SIN	1000-10000 t/år	Ureguleret, cosing (Masking, antioxidant)	Max 3 mg/kg fødevare	Max 3 mg/kg fødevare
4-hydroxybenzosyre	99-96-7	EU COM Cat 1 CoRAP	1000-10.000 t/år	Reguleret som konserveringsmidler	Tilladt som monomer	Tilladt som additiv
Dihydroxybiphenyl	92-88-6	EU COM Cat 1	1000-10000 t/år	Ureguleret, cosing	Max 6	Ikke tilladt

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
				(bleaching, skinprotecting)	mg/kg fødevare	
Styren	100-42-5	EU COM Cat 1 SIN	1.000.000-10.000.000 t/år	Ureguleret, cosing (parfume)	Tilladt som monomer	Tilladt som additiv
Deltamethrin	52918-63-5	EU COM Cat 1	Præregistreret	Ureguleret, cosing (antimicrobial)	Ikke på positive liste	Ikke tilladt
Resmethrin	10453-86-8	EU COM Cat 1	Præregistreret	Ureguleret, cosing (skinconditioning, masking)	Ikke på positiv liste	Ikke tilladt
Triphenyl phosphate	115-86-6	CoRAP SIN	1000-10.000 t/år	Ureguleret, cosing (plasticiser)	Ikke på positiv liste	Max 0,01 mg/kg fødevare
4-nitrophenol	100-02-7	EU COM Cat 2 SIN	Intermediat	Ureguleret, cosing (hårfarve)	Ikke på positiv liste	Ikke tilladt
Hexamethylindanopyran	1222-05-5	EU COM Cat 3b SIN	1000-10.000 t/år	Ureguleret, cosing (masking, perfume)	Ikke på positiv liste	Ikke tilladt
Acetyl hexamethyl tetralin	1506-02-1	SIN	1000-10.000 t/år	Reguleret på bilag III (masking)	Ikke på positiv liste	Ikke tilladt
Tert-butylmethylether (MTBE)	1634-04-4	EU COM-Cat 1 SIN CoRAP	1.000.000-10.000.000 t/år	Ureguleret, cosing (solvent)	Ikke på positiv liste	Max 0,01 mg/kg fødevare
Methylsalicylat	119-36-8	CoRAP	1000-10.000	Ureguleret, cosing	Max 30	Max 30 mg/kg fødevare

Stofnavn	CAS nr.	EU-lister	REACH	Kosmetik	Fødevarekontaktmaterialer	
			t/år	(denaturant, perfuming, soothing)	mg/kg fødevare	
Climbazol	38083-17-9	CoRAP	10-100 t/år	Reguleret som konserveringsmiddel	Ikke på positiv liste	Ikke tilladt
N-(4-Hydroxyphenyl)ethanamid, Paracetamol	103-90-2			Ureguleret, cosing (skinconditioning)	Max 0,05 mg/kg fødevare	Max 0,05 mg/kg fødevare

EU COM liste – EU's liste over potentielt hormonforstyrrende stoffer
COSING – EU-kommissionens database over kosmetiske ingredienser. Ikke juridisk gældende.

Appendix 2

Chemicals omitted from the evaluation of (potential) endocrine disruptors

In the selection phase a number of chemicals from a list proposed by Danish Environmental Protection Agency (EPA) (Appendix 1) have been evaluated, and several were omitted for different reasons. The omitted chemicals are listed below to give an overview of reasons for omission, uncertainties and data-gaps. The omitted chemicals can be grouped according to the following reasons for omission: a) chemicals that are examined but not considered to have an anti-androgenic, estrogenic or thyroid hormone disrupting mode of action (but may be an endocrine disrupter with another endocrine disrupting mode of action); b) chemicals not examined sufficiently with regards to anti-androgenic, estrogenic or thyroid hormone disrupting mode of action; c) chemicals that in cell based studies were found to have anti-androgenic, estrogenic or thyroid hormone disrupting mode of action but in which data are insufficient for DNEL determination; d) chemicals with an anti-androgenic, estrogenic or thyroid hormone mode of action but insufficient exposure data.
For pesticides, an additional criterion for inclusion was the presence on a list of pesticides contributing with the highest hazard quotient (i.e. highest exposure in comparison with ADI) in a paper by Jensen et al., 2015. Pesticides with endocrine disrupting mode of action that were not present on that list are presented below.
In the evaluation of the list on suspected endocrine disrupters provided by Danish EPA (Appendix 1), it can be seen that most of the chemicals were omitted due to reason c) or d). This is an indication that children and the unborn child are likely to be exposed to a number of endocrine disrupting chemicals in addition to those included in this project.

Table on omitted substances in the project on exposure of children and the unborn children to endocrine disrupting (ED) chemicals. Reasons for omission from the cumulative risk assessment in this project are listed. Endocrine disrupting mode of action is indicated using the following letter codes: AA: anti-androgenic mode of action; E: estrogen-like mode of action; T: thyroid hormone disrupting mode of action. For abbreviation of chemicals, see Appendix 1. ED: endocrine disruption. A question mark (?) indicates that no clear conclusions could be obtained on e.g. mode of action or availability of data on toxicity or exposure.

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
		Brominated		
BEH-TEBP/BEHTBP	AA?	No?	Yes, diet and dust.	Omitted due to lack of data on possible ED effects. Present on EPA list because “Health effects are suspected because TBPH is a brominated analogue of di(ethylhexyl) phthalate (DEHP)” (Corap, SIN)
TBBPA oligomer				UVCB, maybe not relevant for exposure assessment.
		Fluorinated		
PFdoDA	T	No. T effect examined in pregnant	?	Omitted due to insufficient data for possible ED effects.

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
		women and fetuses (Wang et al., 2014). Anti-estrogenic at high doses in rat. Data not sufficient for DNEL determination Possible reproductive toxicity at high doses may be due to general toxicity.		
PFunDA	T, E	No. T effect examined in pregnant women and fetuses (Wang et al., 2014; Berg et al., 2015). E in fish (Benninghoff et al., 2011). Data not sufficient for DNEL determination	?	Omitted due to insufficient data for possible ED effects.
PFDA	T, E	No. T examined in pregnant women (Berg et al., 2015) and fetuses. E in fish (Benninghoff et al., 2011; Jo et al., 2014). Data not sufficient for DNEL determination	?	Omitted due to insufficient data for possible ED effects.
PFNA	T, E, AA	No. T examined in pregnant women and fetuses (Wang et al., 2014; Webster et al., 2014). E in fish (Benninghoff et al. 2011; Zhang et al., 2016) and rats (increased estradiol; Feng et al., 2009), but data not sufficient for DNEL determination. Possible AA due to reduced testosterone in male rats, but data not sufficient for DNEL determination.	?	Omitted due to insufficient data for possible ED effects.
PFHpA	?	No	?	Omitted due to lack of data for possible ED effects.
PFPeA	?	No	?	Omitted due to lack of data for possible ED effects.
PFDeA	T	No. T effect in humans	?	Omitted due to insufficient data for possible ED effects.
PFTrDA	E	No. E in fish (Jo et al., 2014). Data not sufficient for DNEL determination		Omitted due to insufficient data for possible ED effects.
PFBA	?	No. Study in mice showed that PFBA did not have the same adverse developmental effects as PFOA and PFOS (Das et al 2008). Lack of examination of ED relevant endpoints	?	Omitted due to lack of data on possible ED effects.
PFBS	?	No. Rat studies by Lieder et al 2009a, 2009b, did not examine ED relevant effects		Omitted due to lack of data on possible ED effects.
PFHxA	?	No. Rat study Klaunig et al. 2015, did not examine ED relevant effects		Omitted due to lack of data on possible ED effects.
Fluorotelomer alcohols	AA, E	No. In vitro studies indicated AA and E effects (Rosenmai et al., 2016). Some of these compounds inhibit testosterone synthesis and some activate estrogen receptors or increase estradiol synthesis. No in vivo data.		Omitted due to insufficient data on possible ED effects.

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
PAPs	AA, E	No. In vitro studies indicated AA and E effects (Rosenmai et al., 2016). Some of these compounds inhibit testosterone synthesis and some activate estrogen receptors or increase estradiol synthesis.		Omitted due to insufficient data on possible ED effects.
Phthalates				
DEP	? (reproductive toxicant, but not by AA mode of action, not T)	?	Yes	Omitted as DEP cannot be grouped with other phthalates (other mode of action).
C6-10, Multi constituent substance: 33% Dioctyl phthalate (117-84-0), 30% Decyl octyl phthalate (119-07-3), 18% Hexyl octyl phthalate (61827-62-1).	AA, T	Yes, no data on the multi constituent substance, but on constituents. More than 0.3% DHxP known to have AA mode of action. 33% DNOP known to have T mode of action.	No exposure data but data on constituents	Omitted as data for constituents are used. Swedish SVHC report (ECHA 2015; reason for inclusion in EPA list) is based on data for constituents.
DIDP	T? AA?	T data only in vitro; insufficient data for DNEL determination. AA in Hershberger assay, but not sufficient for DNEL determination.	Yes	Omitted due to insufficient data for DNEL determination for T effect and uncertainty regarding possible AA effect (other mode of action than other phthalates).
Phenols				
Bisphenol M, Cas 13595-25-0	?	No? No relevant effects in 28 day study; not included in published in vitro studies on bis-phenols.	No? ECHA database: 0-10 tonnes per year	Omitted; not examined for possible ED effect
Dihydroxybiphenyl = 4,4' biphenol	E	No? Only in vitro data on E mode of action. No effect in reproductive toxicity study according to registration dossier (ECHA webpage)	? Plastics	Omitted due to insufficient data on ED effects.
4-nitrophenol	AA, E	Yes. Immature rat Hershberger, uterotrophic, subcutaneous. Data not sufficient for DNEL determination	No? Registration dossier indicates no consumer exposure. Pesticide, but used for production of other chemicals, dyes, diesel	Omitted due to lack of exposure data and insufficient data for ED effects. Biomonitering data can be found.
Preservatives				
4-hydroxybenzoic acid = salicylate	E/AA?	Not examined for ED effects	Medicine. Active compound in acetyl salisylate.	Omitted due to lack of data on possible ED effects. Corap justification for ED

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
				indicates few data
Isobutylparaben	E	Yes, uterotrophic assay (Darbre et al., 2002; Vo and Jeung, 2009)	Not permitted in cosmetics products.	Omitted due to lack of exposure
Pesticides				
Chlorpyrifos	AA, T	Yes. Reduced testis weight and sperm count in rats (Akhtar et al., 2009). Altered thyroid histology, reduced T4 in dams, mice (De Angelis et al., 2009).		Omitted as this pesticide is not present on list in Jensen et al., 2015
Climbazol	?	No. Prolonged gestation is observed in rodents, but this effect is not clearly related to an estrogenic or antiandrogenic mode of action.	In food, but also possible use in cosmetic products	Omitted due to lack of data on ED mode of action
Deltamethrin	E/AA	Maybe. Effects on reproductive organs and sperm quality are seen in male rats, but not clear if related to ED mode of action (Andrade et al., 2002).		Not present on list in Jensen et al., 2015
Imazalil	AA?	No. Only in vitro data for AA effect and reduced steroid synthesis. Other possible endocrine disrupting effects (prolonged gestation and impaired parturition in rats (Dirkx et al., 1992)) are not clearly related to an estrogenic or antiandrogenic mode of action. (see section 7.1.1)		Omitted due to insufficient data on ED mode of action.
Iprodion	AA	Yes. Histological changes in testes, prostate, seminal vesicle, epididymis, rats (Chambers et al., 1992)		Omitted as this pesticide is not present on list in Jensen et al., 2015
Propamocarb	E	Yes. Impaired sperm quality in offspring, reduced weight of epididymis and seminal vesicle, histological changes in rats (Thorsrud et al., 2002)		Omitted as this pesticide is not present on list in Jensen et al., 2015
Resmethrin	?	?		Omitted due to lack of data on ED effects
Tebuconazol	AA	Yes. Nipple retention in male rats (Taxvig et al., 2007)		Omitted as this pesticide is not present on list in Jensen et al., 2015
Thiabendazol	T	Yes. Reduced T3, increased TSH, increased thyroid weight and hyperplasia, rats (Myers et al., 1990; Lankas et al., 1995)		Omitted as this pesticide is not present on list in Jensen et al., 2015
UV-filtres				

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
3-BC, 3-benzylidene camphor	E	Yes	Not permitted in cosmetics products.	Omitted due to lack of exposure
4-MBC, 4-methylbenzylidene camphor	E, T	yes	Not found in survey of Danish products (MST 2015).	Omitted due to lack of exposure
Benzophenone 1	E	Yes	Negligible exposure. Not permitted as UV-filter but as absorber in cosmetic products. Present in five nail polishes in survey of Danish products (MST 2015).	Omitted due to lack of exposure
Benzophenone 2	E, T	Yes	Not permitted as UV filtre in sun screen. Not found in survey of Danish products (MST 2015).	Omitted due to lack of exposure
Benzophenone (BP)	E, T	Only E effect of metabolite in uterotrophic assay in ovariectomized rats. Only in vitro data on T effect.	Yes	Omitted due to insufficient data on possible ED effects. .
Benzophenone 12 (BP12)	-	No. No data on ED effects or reproductive toxicity	Yes	Omitted due to lack of data on possible ED effects.
Octocrylen	Ø?	No. No data on ED effects or reproductive toxicity. Indication of E effect in vitro (Japanese language paper by Matsumoto 2005)	? UV filter	Omitted due to lack of data on possible ED effects.
4-Hydroxycinnamic acid, cas 7400-08-0, p-coumaric acid	T	Not sufficient for DNEL determination. Only on dose applied in rat study.	Possible use in cosmetics. Natural dietary component	Omitted due to insufficient data on possible ED effects and uncertainty on exposure evaluation.
Isoamyl-p-methoxycinnamat	-	No. No data on ED effects or reproductive toxicity. Possible read across to OMC, but this is not further elaborated on in this survey.	?	Omitted due to lack of data on possible ED effects.
Other (personal care)				
Resorcinol	T?	No. Effects on the thyroid observed in older human case studies, effect on TPO inhibition in vitro, some effects in rodents in vivo, but data are not robust enough to derive a	Yes, but negligible exposure (MST 2012)	Omitted due to insufficient data on possible ED effects and negligible exposure

Chemical	Possible mode of action (AA, E, T)	Presence of relevant toxicity data (yes/no)	Relevant human exposure?	Reason for omitting this chemical in the current project
		DNELs.		
Octamethylcyclo-pentasiloxane D5	Other ED mode of action			Omitted as mode of aciton is not relevant for grouping with AA or E chemicals in current project.
Other (industrial chemicals)				
Styrene	-	No ED effects	Yes	Omitted (from ED risk assessment) due to lack of data on possible ED effects. Reproductive toxicity due to other developmental toxicity than endocrine disruption. Included in neurotox section.
Triphenyl phosphate	AA, E?	No. Indications of E and AA effects in vitro (Krivoshiev et al 2016; Kojima et al 2013), testis/ testosterone effect in adult male mice (Chen et al 2015)	Yes? Flame retardant, plastics, rubber. Data for dust, Brommer et al. 2012; Marklund et al. 2003.	Omitted due to insufficient data on possible ED effects.
Hexamethylindanopyran = Galaxolide, cas 1222-05-5	AA?	No. Only in vitro and zebrafish data on possible ED mode of action. Not sufficient for DNEL determination.	? perfume	Omitted due to insufficient data on possible ED effects. No adverse developmental toxicity according to EU RAR 2008 (ECB 2008)
Acetyl hexamethyl tetralin = Tonalide =AHTN	AA?	No. E in vitro, but not in a uterotrophic assay (EU RAR). Not examined for other ED effects	? Parfumestof	Omitted due to lack of data on possible ED effects. Developmental toxicity due to effects on pup body weight according to EU RAR (ECB 2008)
MTBE	(AA?, T?)	ED effects cannot be categorized as being AA or T.	Yes? Drinking water, air, petrol (Ahmed, 2001). High exposure with occupational use.	Omitted due to other ED mode of action than AA, E or T. Possible lack of relevant exposure data for consumers according to EU RAR (ECB 2002)
Methylsalicylat	-	No. No effect in uterotrophic assay and not examined for ED effects in vivo. No effect on estrogen receptors in vitro (Zhang 2012).	Topical analgesics?	Omitted due to lack of data on possible ED effects. Suspected for reproductive toxicity due to similarities with acetylsalicylic acid; i.e. suspected risk of reproductive toxicity is not related to an ED mode of action.

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Appendix 3

Selection of chronic neurotoxic substances

Selection of neuro-toxic substances

Below three lists for identification of neurotoxic substances are included:

- Grandjean og Landrigan (2006+2014),
- Giordano & Costa (2012)
- US EPA´s list of chemicals with Substantial Evidence of Developmental Neurotoxicity

As can be seen from the lists below they include a far greater number of substances as identified in table 2.2 as the substances chosen for the table were selected/screened from a combination of the following criteria:

- the substances have to be documented and generally accepted as chronic neurotoxicants
- data should preferably be available on dose-response relationship and/or on TDI, NOAEL (LOAEL) for the neurotoxic effects
- the substances should be relevant in relation to exposure of the target group of this project (small children and pregnants/foetus)
- advantage should be made from data from previous Danish EPA consumer projects

Further, some specific substances were excluded, based on the following:

Methanol: may induce blindness from acute poisoning (well-known from cases where methanol has been added alcoholic beverages). Such high exposure scenarios to methanol are not considered relevant for this report.

Ethanol: The development neurotoxic properties of ethanol are related to the consumption of alcoholic beverages during pregnancy. Thus, the exposure for this substance is not an unintended exposure but is to be considered as life style related exposure for which recommendations from the National Board of Health already exist.

Arsenic: EFSA (2009) found that available epidemiological studies indicated a relationship between high levels of oral exposures to inorganic arsenic and sensitive end-points for peripheral and central neurotoxicity. Studies in experimental animals have shown that *in utero* exposure to inorganic arsenic via oral administration to the dam causes neural tube defects, fetal growth retardation and neurotoxicity including alteration in lomotor activity, spatial learning and changes in neuroendocrine markers associated with depressive-like behaviors in the offspring. Inhibition of arsenic methylation has been shown to increase its developmental toxicity. Possible mechanisms for arsenic-induced neurotoxicity include changes in the cytoskeletal composition of the peripheral nerve, alterations in neurotransmitter systems and oxidative stress. However, EFSA (2009) concluded that due to the major species differences and insufficient data, direct extrapolation to humans could not be made.

Instead EFSA (2009) concluded skin lesions, cancers of the skin, urinary bladder and lung as the most sensitive end-points from arsenic exposure and identified BMDL01 levels of 0.3 to 8 µg/kg b.w. for these end-points.

Thus, data is not sufficient for identification of NOAELs/LOAEL values or for dose-response assessment of the potential neurotoxic effects from arsenic.

EFSA (2009). Scientific Opinion on Arsenic in Food. EFSA Panel on Contaminants in the Food Chain (CONTAM). European Food Safety Authority (EFSA), Parma, Italy. EFSA Journal 2009; 7(10):1351

Manganese: Only considered neurotoxic in relation to inhalational exposure. Thus, no concern for neurotoxic adverse effects from oral exposure has been addressed (EFSA 2013). There seems to be no data that indicate that inhalational exposure to manganese would be relevant to consider for the target groups of this project.

EFSA (2013). Scientific Opinion on Dietary Reference Values for manganese. EFSA Journal 2013;11(11):3419.

Fluoride: According to SCHER (2011) it remains uncertain to which extent fluoride should be considered as a neurotoxicant, although epidemiological studies have suggested that intake of drinking water with high levels of fluoride may impair the IQ of children. Thus, the evidence is not clear and data seems not sufficient for identification of NOAELs/LOAEL values or for dose-response assessment of the potential neurotoxic effects.
SCHER (2011). Critical review of any new evidence of the hazard profile, health effects, and human exposure to fluoride and the fluoridating agent of drinking water. Adopted by SCHER 16 May 2011.

Lists on neurotoxic substances

Grandjean & Landrigan (2006) in their publication identified 201 chemcials for which they found human evidence for neurotoxicity in humans. To identify environmental chemicals that are toxic to the human brain, they searched the hazardous substances data bank of the US National Library of Medicine, where substances are listed with their adverse effects in human beings. They checked the completeness of this list against other data sources and with a previous review of published data for clinical toxicity. From this they identified the following 201 chemical as human neurotoxicants:

Metals and inorganic compounds

- Aluminum compounds
- Arsenic and arsenic compounds
- Azide compounds
- Barium compounds
- Bismuth compounds
- Carbon monoxide
- Cyanide compounds
- Decaborane
- Diborane
- Ethylmercury
- Fluoride compounds
- Hydrogen sulphide
- Lead and lead compounds
- Lithium compounds
- Manganese and manganese compounds
- Mercury and mercuric compounds
- Methylmercury
- Nickel carbonyl
- Pentaborane
- Phosphine
- Phosphorus
- Selenium compounds
- Tellurium compounds
- Thallium compounds
- Tin compounds

Organic solvents

- Acetone
- Benzene
- Benzyl alcohol
- Carbon disulphide
- Chloroform
- Chloroprene
- Cumene
- Cyclohexane
- Cyclohexanol
- Cyclohexanone
- Dibromochloropropane
- Dichloroacetic acid
- 1,3-Dichloropropene
- Diethylene glycol
- N,N-Dimethylformamide
- 2-Ethoxyethyl acetate

• Ethyl acetate
• Ethylene dibromide
• Ethylene glycol
• n-Hexane
• Isobutyronitrile
• Isophorone
• Isopropyl alcohol
• Isopropylacetone
• Methanol
• Methyl butyl ketone
• Methyl cellosolve
• Methyl ethyl ketone
• Methylcyclopentane
• Methylene chloride
• Nitrobenzene
• 2-Nitropropane
• 1-Pentanol
• Propyl bromide
• Pyridine
• Styrene
• Tetrachloroethane
• Tetrachloroethylene
• Toluene
• 1,1,1-Trichloroethane
• Trichloroethylene
• Vinyl chloride
• Xylene

Other organic substances

• Acetone cyanohydrin
• Acrylamide
• Acrylonitrile
• Allyl chloride
• Aniline
• 1,2-Benzenedicarbonitrile
• Benzonitrile
• Butylated triphenyl phosphate
• Caprolactam
• Cyclonite
• Dibutyl phthalate
• 3-(Dimethylamino)-propanenitrile
• Diethylene glycol diacrylate
• Dimethyl sulphate
• Dimethylhydrazine
• Dinitrobenzene
• Dinitrotoluene
• Ethylbis(2-chloroethyl)amine
• Ethylene
• Ethylene oxide
• Fluoroacetamide
• Fluoroacetic acid
• Hexachlorophene
• Hydrazine
• Hydroquinone
• Methyl chloride

- Methyl formate
- Methyl iodide
- Methyl methacrylate
- p-Nitroaniline
- Phenol
- p-Phenylenediamine
- Phenylhydrazine
- Polybrominated biphenyls
- Polybrominated diphenyl ethers
- *Polychlorinated biphenyls
- Propylene oxide
- TCDD
- Tributyl phosphate
- 2,2',2''-Trichlorotriethylamine
- Trimethyl phosphate
- Tri-o-tolyl phosphate
- Triphenyl phosphate

Pesticides

- Aldicarb
- Aldrin
- Bensulide
- Bromophos
- Carbaryl
- Carbofuran
- Carbophenothion
- α-Chloralose
- Chlordane
- Chlordecone
- Chlorfenvinphos
- Chlormephos
- Chlorpyrifos
- Chlorthion
- Coumaphos
- Cyhalothrin
- Cypermethrin
- 2,4-D
- DDT
- Deltamethrin
- Demeton
- Dialifor
- Diazinon
- Dichlofenthion
- Dichlorvos
- Dieldrin
- Dimefox
- Dimethoate
- Dinitrocresol
- Dinoseb
- Dioxathion
- Disulphoton
- Edifenphos
- Endosulphan
- Endothion
- Endrin

- EPN
- Ethiofencarb
- Ethion
- Ethoprop
- Fenitrothion
- Fensulphothion
- Fenthion
- Fenvalerate
- Fonofos
- Formothion
- Heptachlor
- Heptenophos
- Hexachlorobenzene
- Isobenzan
- Isolan
- Isoxathion
- Leptophos
- Lindane
- Merphos
- Metaldehyde
- Methamidophos
- Methidathion
- Methomyl
- Methyl bromide
- Methyl demeton
- Methyl parathion
- Mevinphos
- Mexacarbate
- Mipafox
- Mirex
- Monocrotophos
- Naled
- Nicotine
- Oxydemeton-methyl
- Parathion
- Pentachlorophenol
- Phorate
- Phosphamidon
- Phospholan
- Propaphos
- Propoxur
- Pyriminil
- Sarin
- Schradan
- Soman
- Sulprofos
- 2,4,5-T
- Tebupirimfos
- Tefluthrin
- Terbufos
- Thiram
- Toxaphene
- Trichlorfon
- Trichloronat

Then in 2014 **Grandjean & Landrigan (2014)** made and update of their previous publication from 2006, and the following substances were added to the list of human neurotoxicants:

- Hydrogen phosphide
- Ethyl chloride
- 1,3 - butadiene

Pesticides:

- Acetamiprid
- Amitraz
- Avermectin
- Emamectin,
- Fipronil (Termidor)
- Glyphosate
- Hexaconazole
- Imidacloprid
- Tetramethylenedisulfotetramine

Giordano & Costa (2012):

Giordano & Costa (2012) considered approximately 200 chemicals as neurotoxic to humans. Of these they focused on the following substances known to be developmental neurotoxicants:

- Methylmercury
- Lead
- Mangenese
- Arsenic
- Ethanol
- Toluene
- Organophosphates (various)
- Organochlorines (dieldrim)
- Herbicides (paraquat)
- Fungicides (maneb)
- PCBs
- PBDEs
- Phthalates
- Bisphenol A

US EPA List of chemicals with Substantial Evidence of Developmental Neurotoxicity:

US EPA (http://investigativereportingworkshop.org/investigations/toxic-influence/story/chemicals-on-list/) (searched April 2016)
Adapted from EPA's list of chemicals with Substantial Evidence of Developmental Neurotoxicity. This list omits most medicines, drugs like LSD and cocaine, and caffeine, but includes food additives.

2-ethoxyethyl Acetate — a solvent, used as a coating for wood, metal and other materials; sometimes found in cosmetics
Acibenzolar-S methyl — a fungicide
Acrylamide — a chemical that is produced naturally in certain foods when they are cooked at high temperatures. It is also manufactured industrially for use in the production of polyacrylamide gels, which are used for various purposes, including the treatment of drinking-water and wastewater; and found in cigarette smoke.
Aldicarb — a pesticide
Allethrin — a pesticide
Aluminum (lactate) — used in lotions to treat very dry skin
Aminopterin — a chemical originally developed for use in cancer treatment.
Arsenic — a semimetallic element, which enters drinking water supplies from natural deposits in the earth or from agricultural and industrial practices.
Aspartame — an artificial sweetener
Benomyl — a fungicide
Benzene — a volatile organic chemical formed through natural processes, such as volcanoes and forest fires. It is also formed from industrial processes, and is used to make plastics, rubber, resins and synthetic fabrics like nylon and polyester. Benzene is also a natural part of crude oil, gasoline and cigarette smoke.
Bioallethrin (s-bioallethrin) — a pesticide
Bis(tri-n-butyltin)oxide — a biocide
Bisphenol A — this chemical is the main ingredient in polycarbonate plastic, used to make water bottles, baby bottles and food storage and heating trays; and epoxy resin, which is used in the lining of most food and beverage cans. Also known as BPA.
Butylated Hydroxy Anisole — a food additive, better known as BHA.
Butylated hydroxytoluene — (BHT) is a toluene-based ingredient used as a preservative in food and personal care products.
Cadmium — a natural element in the earth's crust. It is found in foods, and people can be exposed from smoking cigarettes or breathing cigarette smoke, workplace, water or industrial facilities that release it into the air.
Carbaryl — an insecticide
Carbon monoxide — an odorless and colorless toxic gas
Chlordecone — an insecticide
Chlorine dioxide — a chemical mostly used to disinfect water
Chlorpyrifos — an insecticide
Cypermethrin — an insecticide
DEET — a common ingredient in insect repellents
Deltamethrin — an insecticide
Diazinon — a pesticide
Dieldrin — an insecticide no longer produced in the U.S., but still found in the environment.
Ethanol — grain alcohol, produced from crops such as corn, used as a fuel additive, solvent and other purposes.
Ethylene thiourea — an industrial chemical mostly used to make rubber products, but also in making fungicides and rodenticides.
Fluazinam — a fungicide
Heptachlor — a non-agricultural insecticide; use is now very limited.

Hexachlorobenzene — can be formed as a byproduct during the manufacture of chemicals used as solvents, other chlorine-containing compounds and pesticides. Small amounts of hexachlorobenzene can also be produced during combustion processes such as burning of city wastes. Currently, the substance is not used commercially in the United States.
Hexachlorophene — a disinfectant
Lead — This heavy metal occurs naturally in the earth's crust. It was formerly used as a gasoline additive and was also commonly added to paint. Lead pipes may also contaminate drinking water. Coal-fired power plants and other industrial uses release lead particles into the air.
Lindane — a chemical used to treat scabies and lice
Maneb — a fungicide
Methanol — also known as wood alcohol, an alternative fuel, and other uses
Methylparathion — a pesticide
Monosodium Glutamate — a flavor enhancer, used as a food additive
Nicotine — the addictive drug in tobacco
Methoxyethanol, 2 — an organic compound used mainly as a solvent
Methylmercury — a form of mercury found in contaminated freshwater and salt water fish. It gets into the air when coal, oil or wood are burned as fuel, or when mercury-contaminated wastes are incinerated
Ozone — a gas that occurs both in the earth’s upper atmosphere and at ground level
Paraquat — an herbicide
Parathion (ethyl) — an insecticide
PBDEs — Polybrominated diphenyl ethers, called PBDEs, are used as flame retardants, among other purposes. Some types of PBDEs have been banned, or phased out, but industry has developed others to replace them.
PCBs (generic) — Polychlorinated biphenyls (PCBs) are a group of chemicals that were used as insulation in electrical transformers, and for other industrial purposes. They are no longer manufactured but have persisted in the environment.
Permethrin — an insecticide
Phthalate, di-(2-ethylhexyl) — This phthalate, commonly referred to as DEHP, is found in many plastic products.
Tebuconazole — a fungicide
Toluene — a common solvent, found in many consumer goods, among them: floor polish, moisturing cream, lubricating oils, paint thinners.
Tributyltin chloride — Man-made organic substances containing the metal tin. They are used as pesticides and biocides in marine antifouling paints and in wood preservatives.
Trichlorfon — an insecticide
Trichloroethylene — used as a solvent to clean metal parts and for other industrial processes, often found as a water contaminant.

Appendix 4

Working tables regarding exposure data on the selected substances

Template for tables

Substance name							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Ref 1						**Scoring either:** **+++** **++** **+** **-**	
Ref n							
Overall evaluation regarding exposure data:							

Explanation regarding the use of columns in the tables

Type of study e.g.:

-Reviews (exposure or risk assessments)

-Expert assessments (EFSA, WHO etc)

-Danish EPA report

Metod e.g.:

- biomonitoring
-modelling
-Specific exposure estimations based on analytical-chemical data

Exposure sources:

-food (incl. drinking water)
-cosmetics
-Indoor environment
-toys
-medicines
-other specific products (specify)

(For each source indication of exposure routes (oral, dermal, inhalation (inh))). Not specifically addressed in all references

Exposure contribution/total exposure

Indication of exposure values (mean-typical exposure valuesand high exposure (may be a 95-percentile) exposure.for the specific sources or for the total exposure (mg/kg/d) or (mg/m3). Also specific worst-case exposure situations may be included.

Target groups

Indication of the target group (e.g. infants (< 1 year), toddlers (1-3 years); children (3 years and above), children specific age groups, in general, adults, women or other specific subgroups), Not addressed in all references.

Relevance for exposure estimation in this project, scoring:

+++: excellent data that can be directly used and is considered sufficient for covering the indicated sources and target groups
++: relevant data that can be used/supplement, however still limitations apply e.g. In the case of old data lack of documentation behind the values
+: enough to indicate a potential for exposure but trustworthy quantitative data is missing
-: data considered to be too old/uncertain/or too limited to be used in the further assessment
(one publication may end up with several different scores for the various sources/target groups that are covered)

- ***To be further used in the project for exposure assessment will require scores of +++/ ++ for the specific sources***

Comments

Open field for comments. E.g. if the reference may contain other relevant information for this project e.g. if risk assessment is included in the reference or if further explanation is needed.

Overall evaluation:

Overall evaluation of the data- are data sufficient for exposure assessment in this project. To which extent do the data cover relevant sources for the exposure. Has the substance been found in the Danish EPA database on chemicals in consumer products? Can specific data gaps be identified? Etc.

NB:

It should be noted that the purpose of the tables below has been to identify and make a screening of the most updated and potential relevant literature for further evaluation for performing exposure assessment for the target groups of this project. The table indicate which type of data is covered by the specific references and also identify the most relevant references for further use in this project (references with scores of ++ or +++). Thus, far from all information from the references will be given in the tables below and it will require further in-depth assessment of each reference to identity the most relevant exposure values to be used for the target groups of this project. This further examination and the quantitative choice of exposure values will be done in connection with the work of chapter 6. Also, it should be noted that the tables below should be seen as a working tool of this project and as several individuals have taken part in the fill-out of the tables there may be some differences in the fill-out of the tables concerning the used terminology and the levels of details in the tables. Also as working tables they do not present final results but as said present data that has to be further evaluated.

Tables regarding exposure data on selected substances

Acrylamide							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/total exposure;** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
EFSA (2015)	Expert assessment	From measured levels of acrylamide in food items in EU population exposure	Food (oral) Especially infant food and food items	Total dietary exposure: Median:	Infants, Toddlers Older chil-	+++	Contains also hazard assessment , TDI con-

		estimates were made based on the consumption pattern of the population. Also bio-monitoring data included.	based on potatoes e.g. snack, chips. For adults coffee is an important source.	Infants: 0.8-1.0 µg/kg/d Toddlers: 1.3-1.4 µg/kg/d Adults: 0.5 µg/kg/d 95-percentiles: Infant: 1.8-2.1 µg/kg/d Toddlers: 2.3-2.4 µg/kg/d Adults: 1.0 µg/kg/d	dren Adults		siderations and BMDL-levels and risk assessment
DTU (2015)	Expert assess-ment	From measured levels of acrylamide in food items in DK population exposure estimates were made based on the consumption pattern of the population.	Food (oral) Especially in food items based on potatoes. Further, coffee, cacao, bread as important sources.	Total dietary exposure: Average (aritmetric): Children (4-14 år): 0.33 µg/kg/d Adults: 0.19 µg/kg/d 95-percentiles: Children (4-14 år): 0.89 µg/kg/d Adults: 0.46 µg/kg/d	Children (4-14 år) Adults	+++	
Selected biomonitoring studies							
Boyle et al. (2016)	Research study	Human biomonitoring of volatile organic compounds including acrylamide (urine)	-	Smoking was associated with acrylamide me-tabolites and use of insense in household nearly significant.	Pregnant women (n=488)	+	US study, no exposure calcula-tions
Heudorf et al (2009)	Research study	Human biomonitoring (urine)	-	Exposure calculated to be: Median: 0.54 µg/kg bw/d. 95 perc. 1.91 µg/kg bw/d Significant association with consumption of	5-6 year old chil-dren (n=110)	+++	Study from Ger-many

				French fries were found			
Boettcher et al (2005)	Research study	Human biomonitoring (urine)	-	No exposure calculations. Higher levels found in smokers	Adults (n=29)	+	Study from Germany
Overall evaluation: EFSA (2015) and DTU (2015) together contain sufficient data for exposure assessment on acrylamide. No other significant sources than food is considered relevant to include. For drinking water the limit value of 0.1 µg acrylamide/l may be used as an upper estimate acrylamide has not been found in the Danish EPA´s database on chemicals in consumer products. Also biomonitoring data is available.							

References:

Boettcher et al (2005) Mercapturic acids of acrylamide and glycidamide as biomarkers of the internal exposure to acrylamide in the general population. Mutation Research 580: 167–176

Boyle et al. (2016) Assessment of Exposure to VOCs among Pregnant Women in the National Children's Study. Int. J. Environ. Res. Public Health, 13, 376

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. edition, June 2015

EFSA (2015). EFSA opinion on acrylamide in food. EFSA Journal 2015;13(6):4104.
http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/4104.pdf

Heudorf et al (2009) Acrylamide in children – exposure assessment via urinary acrylamide metabolites as biomarkers. Int. J. Hyg. Environ. Health 212: 135–141

Aluminium and compounds							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/ total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
SCCS (2014)	Expert assessment	Compilation of updated data regarding aluminium exposure from food and exposure estimates regarding exposure from cosmetics in relation to the EU population	Food (oral) Cosmetics (dermal)	Mean exposure, food: Children, 1 year: 0.89 mg/kg bw/week Adults: 0.29 mg/kg bw/week 95-percentiles, food: Children, 1 year: 1.9 mg/kg bw/week Adults: 0.67 mg/kg bw/week For further systemic exposure estimation an oral bioavailability of 0.1 % was used. Cosmetics (as internal dose)): Children, 1 year: 0 mg/kg/week (cosmetics containing Al not considered relevant) Adults: 14.7 µg/kg bw/week (antiperspirant) Adults: 31-32 µg/kg bw/week (antiperspirant, lip stick, lip gloss) (average consumers, given as internal doses with an absorption factor of 0.5% from intact skin). Adults total (Systemic exposure through food and the use of lipstick/lip gloss, antiperspirants and toothpaste): 600 µg/kg bw/week (worst-	Children (various age groups) Adults	+++	Contains also effect assessment, and TDI-level and risk assessment.

				case)			
NSCFS (2013)	Expert assessment	Compilation of data regarding aluminium exposure from food and exposure estimates regarding exposure from cosmetics in relation to the Norwegian population	Food (oral) Cosmetics (dermal)	The estimated exposure taken over by SCCS (2014), see above	Children (various age groups) Adults	+++	Contains also effect assessment, and TDI-level and risk assessment.
Overall evaluation: SCCS (2014) and NSCFS (2013) are considered to contain sufficient data for exposure assessment of aluminium. The primary exposure sources are food (children and adults) and cosmetics (adults). Only few data on aluminium in the Danish EPA database on chemicals in consumer products e.g. in pigments for porcelain and in tooth brushes. No relevant biomonitoring studies were found in search. Also contribution from drinking water using the current Danish limit value of 200 µg Al/l) may be considered							

References

NSCFS (2013). Risk assessment of the exposure to aluminium through food and the use of cosmetic products in the Norwegian population. Norwegian Scientific Committee for food safety. VKM- 05/04/2013

SCCS (2014). OPINION ON the safety of aluminium in cosmetic products. Scientific Committee on Consumer Safety. Opinion adopted at SCCS 5th plenary meeting of 27 March 2014. SCCS/1525/14. Revision of 18 June 2014

BHA							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/ total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
EFSA 2012	Expert evaluation	Exposure assessment to BHA using new comprehensive food consumption database incl food contact materials.	Food (oral)	Food (as additive): Mean range (mg/kg bw/day): 0.04-0.23 for toddlers, 0.08-0.36 for children, 0.03-0.12 for adults. 95th percentile (mg/kg bw/day): 0.14-0.57 for toddlers, 0.26-0.60 for children,	In addition to toddlers, children and adults, there are data for	+++	Range determines differences between European countries. BHA in food contact materials may

				0.08-1.12 for adults. Food contact materials additionally: 2.5 for toddlers, 1.3 for children, 0.43 mg/kg bw/day for adults (conservative estimates, but actual measures in food contact materials seem to be missing).	adoles-cents and elderly.		contribute sub-stantially to total exposure to BHA and exceed ADI for children/ tod-dlers.
Mancini 2015	Research paper	Conservative approach combining consumption data and maximum permitted levels of several additives including BHA and BHT in toddlers	Food (oral)	Toddlers less than 3 years old in France: 0.39 mg/kg bw/day	Toddlers	+++	France
NTP 2014	Expert evaluation			1975 data: estimated intake 4.3 mg per person or <0.01 mg/kg bw per day (ref to IARC)		+	Old exposure data
IARC 1986	Expert evaluation			1975 data: estimated intake 4.3 mg per person or <0.01 mg/kg bw per day		+	Old exposure data
Soubra 2006	Research paper	Combination of food con-sumption data and measured levels of BHA and BHT	Food (oral)	Exposure calculations for children 9-18 years old	Children	++	Lebanon
Danish "Tænk" da-tabase (The Con-sumer Council 2016)			Cosmetic (dermal)	Allowed in cosmetics as antioxidant/masking if a safe use can be documented by the manufac-turer. The Danish TÆNK-data base contains infor-mation about specific cosmetics product on the market that according to the label on the product contain BHA.			Further infor-mation on quanti-tative exposure from cosmetics not available
Overall evaluation: The data from EFSA 2012 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. However, data							

for exposure from food contact materials seem to be missing, No data on human biomonitoring found in pubmed search. No data available on use in cosmetics or pharmaceutical (EFSA 2011 states the use as antioxidant in cosmetics and pharmaceuticals). BHA was not found in the Danish database on consumer products. Information on use of BHA in cosmetics products in TÆNK-database.

References:

EFSA Journal 2011;9(10):2392. Scientific Opinion on the re-evaluation of butylated hydroxyanisole – BHA (E 320) as a food additive.

EFSA Journal 2012;10(7):2759. SCIENTIFIC OPINION Statement on the safety assessment of the exposure to butylated hydroxyanisole E 320 (BHA) by applying a new exposure assessment methodology.

IARC 1998. International Agency for Research on Cancer (IARC) - Summaries & Evaluation. BUTYLATED HYDROXYANISOLE (BHA) VOL.: 40 (1986) (p. 123).

Mancini FR, Paul D, Gauvreau J, Volatier JL, Vin K, Hulin M. Dietary exposure to benzoates (E210-E213), parabens (E214-E219), nitrites (E249-E250), nitrates (E251-E252), BHA (E320), BHT (E321) and aspartame (E951) in children less than 3 years old in France. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2015;32(3):293-306.

NTP 2014. National Toxicology Program Report on Carcinogens, Thirteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. http://ntp.niehs.nih.gov/pubhealth/roc/roc13/

Soubra L, Sarkis D, Hilan C, Verger P. Dietary exposure of children and teenagers to benzoates, sulphites, butylhydroxyanisol (BHA) and butylhydroxytoluen (BHT) in Beirut (Lebanon). Regul Toxicol Pharmacol. 2007 Feb;47(1):68-77. Epub 2006 Sep 20.

BHT							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/ total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
EFSA 2012	Expert evaluation	Conservative approach combining consumption data and maximum permitted levels of BHT	Food (oral)	Food (as additive) (mg/kg bw/day): Mean range (mg/kg bw/day): 0.01-0.09 for children, 0.01-0.03 for adults. 95th percentile (mg/kg bw/day): 0.05-030 for children, 0.03-0.17 for adults. Food contact materials additionally (mg/kg bw/day): 0.2 for children, 0.05 for adults. (Conservative estimate, no specific data for food contact materials)	Children 3-9 years, Adults 18-64 years	+++	BHT in food contact materials may contribute substantially to total exposure to BHA and exceed ADI for children (conservative approach).
MST 2009	Danish EPA report	Survey and chemical analysis in selected products	Diapers and jackets	Detection of BHT in diapers and jackets. Apparently no calculated exposure values	2-year olds	++	Lack of calculated exposure (?). Overview of data in several EPA surveys from 2002-2009
MST-LOUS 2013	Danish EPA report	Survey on exposure to alkylphenols and -epoxylates		Very limited information on BHT applications, no calculated data on exposure		+	
MST database	Danish EPA	Surveys and chemical analysis in selected products		In the Danish database on consumer product many products containing BHT are found, and it		+/+++	

	reports			may be possible to identify products relevant to children and possibly the unborn child. If relevant data is obtained by further examination of the database these will be included for exposure assessment.			
Mancini 2015	Research paper	Conservative approach combining consumption data and maximum permitted levels of several additives including BHA and BHT in toddlers	Food (oral)	Toddlers less than 3 years old in France	Toddlers	+++	France
Soubra 2006	Research paper	Combination of food consumption data and measured levels of BHA and BHT	Food (oral)	Exposure calculations for children 9-18 years old	Children/teenagers	++	Lebanon
Vin 2013	Research paper	Conservative approach combining consumption data and maximum permitted levels of several additives including BHA and BHT in toddlers, children and adults	Food (oral)	Exposure calculations for several age groups Children 1-4 years (data from 1992): Mean : 0.003-0.052 95-perc: 0.028-0.202	Toddlers, children, adults	++(+)	France, UK, Ireland and Italy
CIR review 2002	Evaluation by Cosmetic Ingredient Review Expert Panel	Review of BHT toxicity and toxicokinetics	Cosmetics	Not clear if exposure data are available			
Danish			Cosmetic	Allowed in cosmetics as antioxidant/masking if a			Further infor-

"Tænk" database (The Consumer Council 2016)				safe use can be documented by the manufacturer. The Danish TÆNK-data base contains information about specific cosmetics product on the market that according to the label on the product contain BHT.			mation on quantitative exposure from cosmetics not available
Overall evaluation: The data from EFSA 2012 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. In the Danish database on consumer product many products containing BHT are found, and several products including diapers may be relevant to children and possibly the unborn child. This may warrant further examination. No data on human biomonitoring found in pubmed search. No data available on use in cosmetics or pharmaceutical (EFSA 2011 states the use as antioxidant in cosmetics and pharmaceuticals). Information on use of BHT in cosmetics products in TÆNK-database.							

References:

EFSA 2012: Scientific Opinion on the re-evaluation of butylated hydroxytoluene BHT (E 321) as a food additive. EFSA Journal 2012;10(3):2588

Lanigan RS, Yamarik TA. Final report on the safety assessment of BHT(1). Int J Toxicol. 2002;21 Suppl 2:19-94.

Mancini FR, Paul D, Gauvreau J, Volatier JL, Vin K, Hulin M. Dietary exposure to benzoates (E210-E213), parabens (E214-E219), nitrites (E249-E250), nitrates (E251-E252), BHA (E320), BHT (E321) and aspartame (E951) in children less than 3 years old in France. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2015;32(3):293-306.

MST-LOUS 2013: Survey of alkylphenols and alkylphenol ethoxylates. Part of the LOUS-review. Environmental project No. 1470, 2013

MST 2009: Kortlægning af kemiske stoffer i forbrugerprodukter Nr. 103 2009. 2-åriges udsættelse for kemiske stoffer.

Soubra L, Sarkis D, Hilan C, Verger P. Dietary exposure of children and teenagers to benzoates, sulphites, butylhydroxyanisol (BHA) and butylhydroxytoluen (BHT) in Beirut (Lebanon). Regul Toxicol Pharmacol. 2007 Feb;47(1):68-77. Epub 2006 Sep 20.

Vin K, Connolly A, McCaffrey T, McKevitt A, O'Mahony C, Prieto M, Tennant D, Hearty A, Volatier JL. Estimation of the dietary intake of 13 priority additives in France, Italy, the UK and Ireland as part of the FACET project. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2013;30(12):2050-80.

Bisphenol A							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/ total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
EFSA 2015	Expert evaluation	3 methods –external, internal, aggregated. For internal exposure estimates EFSA comprehensive data base was combined with concentration data from literature and EFSA data.	Diet, Cosmetics, Toys, Dust, Thermal paper (various exp routes)	All figures in ug/kg bw/day: Total internal exposure (aggregated, average): 0.384 in toddlers, 0.140 in women of childbearing age, 0.172 in adolescents. Total internal exposure (aggregated, high): 0.88 in toddlers, 0.45 in women of childbearing age, 0.47 in adolescents. Dietary external intake up to 0.857 in infants and toddlers, 0.388 in women of childbearing age, 1.4 in adolescents. Specific dietary exposure for Denmark is presented for specific age groups. Cosmetics: data for dermal exposure at all ages Toys: exposure data for toddlers Dust: exposure data for all ages Thermal paper: exposure data for all ages excluding infants (toddlers)	Infant (several groups), toddlers, adolescents, women of childbearing age	+++	Biomonitoring data in line with estimated internal exposures (“backward modelling”). Biomonitoring data up to 2012 included. More recent data can be found.

				External and internal aggregated exposure - for specific figures please see the following tables: In EFSA (2015) Table 22 and 23 lists external exposure values for all sources, several age groups (mean and high) Table 31 and 33 lists internal exposure values for all sources, several age groups (mean and high)			
ECHA 2015	Expert evaluation	RAC/SEAC opinion on restriction of BPA in thermal paper	Thermal paper (dermal)	Exposure data for thermal paper: median 10 ng/kg bw/day; 95th percentile 50-80 ng/kg bw/day. Exposure from other sources: data from French diet study applied: mean 1.36 ng/kg bw/day, high 3.8 ng/kg bw/day.	Pregnant women handling thermal paper	+++	
MST 2015	Danish EPA report	Survey and experimental study on BPA release from polycarbonate		No exposure estimates	-	+	Lack of calculated human exposure
MST 2011	Danish EPA report	Calculated exposure based on migration analyses and data for presence of BPA	Thermal paper (dermal), baby dummies/pacifiers (dermal and oral)	Bisphenol A detected. Exposure estimates for dermal and oral exposure (see report for specific figures)	Children, adults	+++	
MST 2009	Danish EPA report	Survey and chemical analysis of selected products	Products, indoor dust, food (oral)	Bisphenol A detected in baby pacifiers. Exposure estimates for several sources (mean and high)	Children 2 years old	+++	
MST 2003	Danish EPA report	Survey and chemical analysis of selected products		Bisphenol A below detection limit in paper towels and toilet paper		-+	Too old data
MST 2002	Danish EPA report	Survey and chemical analysis of selected products		Bisphenol A not detected in sanitary towels		-+	Too old data

MST 2006	Danish EPA report	Survey and chemical analysis of selected products		Bisphenol A detected in sex toys		+	Too old data
Selected biomonitoring studies							
Frederiksen 2013a	Research study	Biomonitoring, Denmark		No exposure estimates	Children and adolescents	+	Lack of calculated human exposure
Frederiksen 2013b	Research study	Biomonitoring, Denmark		Exposure calculations for BPA Mean (ug/kg bw/day): 0.04 for children, 0.03-0.04 for adult women 95th percentile (ug/kg bw/day): 0.14-0.21 for children, 0.12-0.24 for adult women	Adult women, children 6-11 years	+++ (adult)	
Covaci 2015	Research study	Biomonitoring, Denmark and other European countries		Mean (ug/kg bw/day): 0.039 for children, 0.036 for adult High (ug/kg bw/day): 0.047 for children, 0.043 for adult	Children 6-11 years, Adult women	+++	
Larsson 2014	Research study	Biomonitoring, Sweden, Parabens, phthalates, bpa, triclosan		No calculation of exposure, but urinary concentrations	Adult women, children 6-11 years	+	Lack of calculated exposure
Overall evaluation: The data from EFSA 2015 and MST 2011 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. In the Danish database on consumer product many products containing bisphenol A are found, however, the highest exposure potential was found from baby dummies/pacifiers and thermal paper. Due to recent elaborate expert evaluation of exposure from different sources was performed by EFSA, searches for other exposure data are limited to recent Danish/Scandinavian exposure data.							

References:

Covaci A, Den Hond E, Geens T, Govarts E, Koppen G, Frederiksen H, Knudsen LE, Mørck TA, Gutleb AC, Guignard C, Cocco E, Horvat M, Heath E, Kosjek T, Mazej D, Tratnik JS, Castaño A, Esteban M, Cutanda F, Ramos JJ, Berglund M, Larsson K, Jönsson BA, Biot P, Casteleyn L, Joas R, Joas A, Bloemen L, Sepai O, Exley K, Schoeters G,

Angerer J, Kolossa-Gehring M, Fiddicke U, Aerts D, Koch HM. Urinary BPA measurements in children and mothers from six European member states: Overall results and determinants of exposure. Environ Res. 2015 Aug;141:77-85

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Bisphenol F							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific spurces / total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST 2014	Danish EPA report	Review of data on use of BPS, BPF (and other BPA analogues) in thermal paper		No exposure estimates		+	Lack of calculated exposure
Liao 2013	Research paper	Measurement in food and calculation of exposure	Food (oral)	7-70 ng/kg bw/day for several age groups (see paper for specific figures)	Children adult	+++	US
Grumetto 2013	Research paper	Analysis of BPF (and other BPA analogues) in milk	Food (oral)	No exposure estimates		+	Presence of BPF in 56% of commercial milk samples (plastic bottles, Italy)
Cao 2015	Research paper	Analysis of BPF (and other BPA analogues) in canned tuna	Food (oral)	No exposure estimates		+	Presence of BPF in 8% of canned tuna samples, Canada
Zoller 2016	Research paper	Analysis of BPF in mustard as naturally occurring compound	Food (oral)	No exposure estimates (may be possible to calculate human intake)		+	“The consumption of a portion of 20 g of mustard can lead to an intake of 100-200 µg of BPF.”

							Swiss data
Pivnenko 2015	Research paper	Analysis of BPF and BPS in household waste paper		No exposure estimates		+	Denmark. Presence of BPF and BPS in food boxes
Selected biomonitoring studies							
Ye 2015	Research paper	Urinary concentrations, no exposure calculations		No exposure estimates	Adult	+	US, lack of calculated exposure
Andra 2015	Research paper	Review of biomonitoring data including urinary concentrations, no exposure calculations		No exposure estimates	Adult	+	US, lack of calculated exposure
Overall evaluation: One paper calculated exposure for children and adults and these data may be useful for making exposure estimates for this project. As very limited data on exposure were available, US data on food content was included. Thermal paper and food are possible sources of exposure, but other sources of exposure have not been examined.							

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Bisphenol S							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources / total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST 2014	Danish EPA report	Survey of data on use of BPS, BPF (and other BPA analogues) in thermal paper	Thermal paper (Dermal/oral)	Although bisphenol S and BPA are structurally similar, the migration into artificial sweat is much higher for bisphenol S with respect to amounts (2.3µg/cm2 for BPA and 6.6 µg/cm2 for bisphenol S) as well as percentage of total content. (3.8% of total for BPA and 10.2% of total for bisphenol S).		+/++	Lack of calculated exposure
Liao 2013	Research paper	Measurement in food and calculation of exposure	Food (oral)	1-5 ng/kg bw/day for several age groups (see paper for specific figures)	Children adult	+++	US
Pivnenko 2015	Research paper	Analysis of BPF and BPS in household waste paper	(food)	No exposure estimates		+	Denmark. Presence of BPF and BPS in food boxes
Gallart-Ayala et al., 2011	Research paper	Measurement of Bisphenol S in food can	Food (oral)	No exposure estimates		+	Lack of calculated exposure
Vinas et al., 2010	Research paper	Measurement of Bisphenol S in food can	Food (oral)	No exposure estimates		+	Lack of calculated exposure
Liao et al., 2012	Research paper	Measurement of Bisphenol S in paper	Thermal receipt paper (dermal)	No exposure estimates		+	Lack of calculated exposure
Selected biomonitoring studies							

Ye 2015	Research paper	Urinary concentrations, no exposure calculations		No exposure estimates	Adult	+	US, lack of calculated exposure
Andra 2015	Research paper	Review of biomonitoring data including urinary concentrations, no exposure calculations		No exposure estimates	Adult	+	US, lack of calculated exposure
Overall evaluation: One paper calculated exposure for children and adults and these data may be useful for making exposure estimates for this project. As very limited data on exposure were available, US data on food content and biomonitoring was included. Thermal paper and food are possible sources of exposure, but other sources of exposure have not been examined.							

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Brominated flame retardants **HBCDD, TBBPA, BDE-47, BDE-99 and BDE-209**							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/ total exposure;** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
DTU (2015)	Expert evaluation	Exposure estimations of calculations based on the results of analysis of various chemical contaminants in foods on the Danish market in the time period 2004-2011 and dietary exposure data collected in a survey in 2005-2008. The exposure to ΣHBCDD is based on measurements in fish from the Danish waters.	Food (oral) Fish Cod liver, salmon, herring, mackerel	Results also reported in LOUS review: Total dietary exposure to ΣHBCDD (mean): Children: 0.23 ng/kg bw/day Adults: 0.19 ng/kg bw/day Total dietary exposure to ΣHBCDD (95-perc.): Children: 1.28 ng/kg bw/day Adults: 0.75 ng/kg bw/day	Various age groups e.g. Infants Toddlers Adults	+++	MOEs are calculated for children and adults and it is concluded that there is no food safety concern.
Danish EPA (2014)	LOUS review	Overall compilation of data. Identification of sources and exposure with focus on the Danish population. Includes data on PBDEs, HBCDD, TBBPA and other BFRs.	Food (oral) *For infants and toddlers*: Breast feeding Food for infants and small children Highest for BDE-47, -99, -153 and -	Infant daily exposure from human milk (BDE-209) Average milk consumption: 0.96-13.3 ng/kg bw/day High milk consumption: 1.44-20.0 ng/kg bw/day Total dietary exposure: (mean from EU surveys) BDE-209	Various age groups e.g. Infants Toddlers Adults	+++	

			209, *For adults:* Animal and vegetable fats, milk and dairy products. Highest for BDE-47 and BDE-209 Fish and seafood (HBCDD) Inhalation of particles Dust Air Soil Placental transfer/fetal exposure	Adults: Average consumer: 0.35 - 2.82 ng/kg bw/day High consumer: 0.7-4.58 ng/kg bw/day Children: 3-6 times higher than that for adults HBCDD exposure from fish, Denmark (for EU estimations see report): Total dietary exposure (mean): Children: 0.23 ng/kg bw/day Adults: 0.19 ng/kg bw/day Total dietary exposure (95-perc.): Children: 1.28 ng/kg bw/day Adults: 0.75 ng/kg bw/day HBCDD from dust Children (using 95-perc concentration of HBCDD): Typical scenario (50 mg dust/day): 5.9 ng/kg bw High end scenario (200 mg dust/day): 330 ng/kg bw For estimates for other BFR see report. Studies report findings of BFRs in umbilical cord blood. No exposure calculated but levels reported.			
EFSA (2012)	Expert	The exposure to brominated	Food (oral)	Report also reviewed in LOUS review.	Various	+++	The panel identi-

	evaluation	phenols and their derivatives (other than TBBPA) from food was estimated. However, due to limited data, only 2,4,6-TBP was included in the risk assessment.	*For infants and toddlers*: Breast feeding *For adults:* Fish and seafood		age groups e.g. Infants Toddlers Adults		fies a NOAEL of 100mg/kg bw/day for 2,4,6-TBP and concludes that the current dietary exposure to 2,4,6-TBP is unlikely to raise a health concern. They further conclude that exposure to infants via breast feeding is not likely to raise a health concern
EFSA (2012b) Novel BFRs	Expert evaluation	The exposure and risk to novel BFRs could not be assessed due to limited data and knowledge on the compounds	Food (oral)		Children various age groups Adults	+	
EFSA (2011) HCBDSs	Expert evaluation	The dietary exposure to hexabromocyclododecanes (HBCDDs) was estimated based contents analysed in food samples and dietary consumption of relevant food items	Food (oral) *For infants and toddlers*: Breast feeding *For adults:* Fish and seafood	Report also reviewed in LOUS review. Exposure was estimated for several EU countries: DK total dietary exposure to ΣHBCDD (mean): Children (3-10 yrs): 0.34-1.27 ng/kg bw/day Adults: 0.14-0.43 ng/kg bw/day	Various age groups e.g. Infants children Adults.	+++	Dietary exposure in infants and toddlers was not performed due to lack of data in the relevant food group.

			Animal and vegetable fats, milk and dairy products.	Total dietary exposure to ΣHBCDD (95-perc.): Children: 1.0-2.42 ng/kg bw/day Adults: 0.39-0.88 ng/kg bw/day			
EFSA (2011b) PBDEs	Expert evaluation	The dietary exposure to polybrominated diphenyl ethers (PBDEs) was estimated based contents analysed in food samples and dietary consumption of relevant food items	Food (oral) *For infants and toddlers*: Breast feeding Food for infants and small children Highest for BDE-47, -99, -153 and -209, *For adults:* Animal and vegetable fats, milk and dairy products. Highest for BDE-47 and BDE-209	Results for dietary exposure are reported in LOUS review (see above). For more details se report. Total dust exposure BDE-209: Young children: 0.5-80 ng/kg b.w.	Various age groups e.g. Infants Toddlers Adults	+++	The CONTAM Panel concluded that current dietary exposure to BDE-47, -153 and -209 in the EU does not raise a health concern; however for the exposure to BDE-99 in children aged 1-3 years of age the CONTAM Panel concluded that there is a potential health concern with respect to current dietary exposure.
EFSA (2010) PBBs	Expert evaluation	The exposure to PBBs from food was estimated based on analysis of 794 food samples	Food (oral) *For infants and toddlers*:	Report also reviewed in LOUS review. Infant daily exposure from human milk High milk consumption: 0.96-1.4 ng/kg bw/day	Various age groups e.g. Infants	+++	The panel concludes that the risk of dietary exposure to PBBs

			Breast feeding *For adults:* Fish and seafood	Total dietary exposure (upper bound): Adults: 0.15 ng/kg bw/day	Toddlers Adults		is of no concern and that it is a low priority as it is no longer produced and environmental concentrations are declining.
Hoffmann et al (2015)	Research paper	Measurements of PBDEs in hand wipes and dust samples from adult volunteers in North Carolina US	Dust -	No exposure calculations but measurements in ng/g	Adults House-holds	++	
Harrad et al (2006)	Scientific paper	Measurements of PBDEs (and PCBs) in dust samples from homes and calculated estimation of exposure dust ingestion, inhalation and diet	Food (oral) Dust (oral) Air (inhalation)	Total daily exposure (air, dust food) to PBDEs with high dust consumption (mean): Toddlers: 95.1 ng/day Adults: 114.1 ng/day Total daily exposure (air, dust food) to PBDEs with high dust consumption (95-perc): Toddlers: 170.6 ng/day Adults: 158 ng/day	Toddlers Adults	+++	
Selected biomonitoring studies							
Mørck et al (2015)	Research study	Human biomonitoring (PBDEs)	-	No exposure calculations but plasma measurements in ng/g lipid	Children 6-11 years And their mothers (n= 290)	+	DK study

Kim et al (2014)	Scientific review paper	A systematic review of bio-monitoring studies on the health impacts of exposure to BFRs in humans, with a particular focus on children was per-formed	All	No exposure calculations but summary of levels from biomonitoring studies.	Various age groups e.g. Infants Toddlers Adults	++	
Vorkamp et al (2009)	Research paper	Human biomonitoring (PBDEs)	-	No exposure calculations but serum measure-ments in pg/mL, ng/g lipid, and pmol/g lipid.	Pregnant women (n=98)	+	DK study
Overall evaluation: The data from Danish EPA (2014), EFSA opinions (2010, 2011a, b, c, 2013) and DTU Food (2015) contain updated data of high quality and the data are consid-ered sufficient for making exposure estimates for this project. Primary exposure is through the diet and especially the intake of fish and other seafood products, animal fat and milk and dairy products. Analysis of TBBPA and HBCDD in food (for small children in particular) may be relevant to include in the project as data on this is lacking. Due to phase out of PBB and negligible exposure levels PBB will not be considered further. Due to lack of data novel BFR's will also not be considered further.							

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Chlorinated solvents (monochloromethane; dichloromethane; trichloroethylene; tetrachloroethylene)							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/ total exposure;** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Danish EPA (2016a)	Project report	Exposure and risk assessment was made for children´s room with respect to evaporation of VOC from building materials, furniture and toys. Exposure estimates were calculated based on measured emission rates of VOCs from various articles	Indoor air in homes (inh) Swim articles (inh) Newly painted surface (inh) Indoor air in homes (inh)	*Trichloroethylene :* Average content of 1 µg/m3 with a 95th percentile value of 7.4 µg/m3 based on indoor measurements in France during 2003-2005. Swim articles: room conc. of 2.8 µg/m^3 Painted surface: room conc. of 2.8 µg/m^3 *Tetrachloroethylene* Indoor: average content of 1.4 µg/m3 with a 90th percentile value of 5.2 µg/m3 based on indoor measurements in France during 2003-2005. Data from 24 homes in DK without known sources:	All age groups in indoor environment	+ +++ +++	Contains also hazard and risk assessment of the emissions considering children´s increased susceptibility to neurotoxic substances

			Dry cleaned clothes (inh) Sources could not be identified	<table><tr><th>Concentration level of tetrachloroethylene</th><th>Number of measurements</th><th>Percentage</th></tr><tr><td><0.02 -0.10 µg/m3</td><td>16</td><td>66 %</td></tr><tr><td>0.11 -0.25 µg/m3</td><td>2</td><td>8 %</td></tr><tr><td>0.26 -1.0 µg/m3</td><td>3</td><td>13 %</td></tr><tr><td>1.1 – 3.0 µg/m3</td><td>3</td><td>13 %</td></tr><tr><td>Total</td><td>24</td><td>100 %</td></tr></table> Exposure level from freshly dry cleaned clothes: the first two weeks an average level of 92 µg/m3 in a room in a poorly ventilated, small apartment, and 13 µg/m3 in a room in an average house. In other part of the homes the average level during the first 14 days were 27 µg/m3 and 5 µg/m3 in the apartment and in the house, respectively. *Monochloromethane and dichloromethane* For these substances there are no data related to indoor air levels. As for trichloroethylene and tetrachloroethylene, there has been focus on these substances and the use of these because of suspected carcinogenic effect of the substances. Thus, the levels of these substances in indoor air are not considered to be higher than those for tri- and tetrachloroeth-		+++ -	

				ylene.			
ATSDR (2015)	Web-site	Toxic substances portal on trichloroethylene http://www.atsdr.cdc.gov/phs/phs.asp?id=171&tid=30	Indoor environment Soil Drinking water Food	Indicate indoor air, polluted drinking water and soil as primary exposure sources whereas exposuere from food may occur at lower levels	Children and adults	+	
Danish EPA (2014)	Project report	Compilation of data for a background document for establishing a health based air quality criteria. Exposure data compiled from the EU Risk Assessment report from 2007.	Dry cleaned cloth (inhalation, dermal)	Refer back to data from the EU Risk Assessment report from 2007: A worst-case scenario would be a consumer exposed daily from wearing freshly dry-cleaned clothes (46 mg/day equivalent to 0.66 mg/kg bw/day for a 70 kg individual), and who also lives in the vicinity of a dry-cleaning establishment and consuming food stored in the vicinity (1.45 mg/kg bw/day), which is equivalent to a total of 2.11 mg/kg bw/day.	Adults	++	
Selected biomonitoring studies							
Boyle et al. (2016)	Research study	Human biomonitoring of Volatile organic compounds including trichloroethylene and tetrachloroethylene (urine)	-		Pregnant women (n=488)	+	US study, no exposure calculations
Overall evaluation: Based on the collected data tetrachloroethylene is considered as the substance with the highest exposure potential and also most exposure data pertains to this substance. In the Danish EPA data base on substances in consumer product tetrachloroethylene has been found in only few products and at very low exposure levels. Data on trichloroethylene and monochloromethane was not found in the database whereas dichloromethane was found in textile colours up to 130 mg/kg. Exposure to trichloroethylene was consid-							

ered to be very limited and the substance is also subject to REACH authorisation which very much will limit the current exposure. No relevant human biomonitoring studies was identified from Denmark or similar countries

For this project it only seems relevant to include tetrachloroethylene in further exposure and risk assessment of the target groups.

References

ATSDR (2015) Toxic substances portal on trichloroethylene http://www.atsdr.cdc.gov/phs/phs.asp?id=171&tid=30

Boyle et al. (2016) Assessment of Exposure to VOCs among Pregnant Women in the National Children's Study. Int. J. Environ. Res. Public Health, 13, 376

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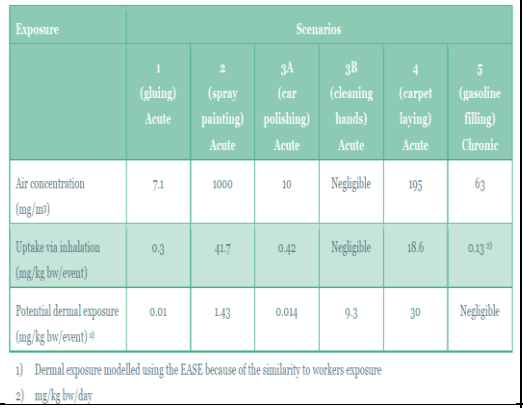
Danish EPA 2016a).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

Hydrocarbons (n-hexane + various isomers of C7 – C12 hydrocarbons)							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/ total exposure;** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Danish EPA (2016a)	Project report	Exposure and risk assessment was made for children´s room with respect to evaporation of VOC from building materials, furniture and toys.	Building material Furniture Toys and articles in a child room (inhalation)	Specific exposure figures from various articles for C6-C12 hydrocarbons were estimated. Real world measurements from children rooms in private homes considered most relevant for this study as higher levels of hydrocarbons	1-3 year old children Children various	+++ +++	Contains also hazard and risk assessment of the emissions considering children´s increased suscep-

		Exposure estimates were calculated based on measured emission rates of VOCs from various articles		were measured compared to calculated exposure based on emission rates. Painting with markers: 38 µg/m^3 toluene (measured during activity) Ironing plastic beads: 30.7 µg/m3 (n-decane + n-undecane, measured during acitiviy) Mock-up children´s room: 2.5 µg/m3 toluene; 2.5 µg/m3 xylenes Emission from paint and lacquer: 3.3 µg/m3 toluene; 39 µg/m3 xylene; 230 µg/m3 sum of hydrocarbons Emission from other articles: 9.1 µg/m3 sum of toluene; 30.5 µg/m3 sum of xylenes; 81.7 µg/m3 sum of hydrocarbons. Values obtained from emission 24 hours after unpacking the products.	age groups Children and adults	+++	tibility to neurotoxic substances
			Indoor air in homes and public buildings (inhalation)	The report compile measured data on hydrocarbons from homes and public buildings in various European countries. (the report contain large tables with hydrocarbon emission levels and calculated exposure levels not easily to include in this table)		+++	
			Food (oral) and food packing material	1-3 year-old: 6 µg styrene/ day		+++	

Danish EPA (2016 b)	Project report	Measurement of emissions from carpets for children´s room and estimation of exposure levels	Carpets (inhalation)	Exposure estimates TABEL 21. RISIKOVURDERING AF AFGASNING FRA UDVALGTE TÆPPER MED STØRSTE AFGASNING. ANGIVELSE AF EKSPONERINGSNIVEAUER, TOLERABELT EKSPONERINGSNIVEAU OG RCR-VÆRDIER Kritiske komponenter, Udvalgte tæpper, areal* / Koncentration i børneværeelse 24 timer* (µg/m³) / Tolerabelt eksponeringsniveau (µg/m³) / RCR Kulbrinter (data tabel B3.14) Tæppe T14 (kunstuld/jute) areal 2,8 m² Heptan 0,32 -* Toluen 0,64 700 0,0009 Sum, C7-C12 kulbrinter 66,6 - Sum af alifatiske kulbrinter C7-C12 61,1 - Sum af aromatiske kulbrinter C7-C12 5,44 1400 0,004	Children 1-3 years	+++	Contains also hazard and risk assessment of the emissions considering children´s increased susceptibility to neurotoxic substances
Danish EPA (2014a)	LOUS survey on n-hexane	Contains among others a compilation of data regarding products containing n-hexane and direct and indirect exposure of the population	Various articles/ products (inhalation) Cuddly toy (emission 16 µg/m3). Adhesives (content up to 30%) Outdoor air Indoor air	 Copenhagen: 0.16 µg/m³ - -	General population	+	

<table>
<tr><td></td><td></td><td></td><td>Food and drinking water (insignificant)</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Danish EPA-LOUS (2014b)</td><td>LOUS survey on toluene</td><td>Contains among others a compilation of data regarding products containing toluene and direct and indirect exposure of the population</td><td>Glue (ind, derm) 1
Spray paint (inh) 2
Car polish (inh, derm)3A
Solvents as cleaning agent (derm) 3A
Carpet glue (inh, derm) 4
Gasoline (inh) 5</td><td>Exposure from scenarios 1-5: 
</td><td>adults</td><td>+++</td><td></td></tr>
<tr><td>Danish EPA-LOUS (2014c)</td><td>LOUS survey on styrene</td><td>Contains among others a compilation of data regarding products containing styrene and direct and indirect exposure of the population</td><td>Food (oral)
Chewing gum (oral)
Carpet (inhalation)
Resins (inhalation/dermal)
Smoking/passive smoking (inhalation)</td><td>Exposure from long-term low-level sources is therefore made up of the following components:
- Emissions from polymeric building materials, incl. carpets (inhaled) - 5 µg/m³ (80 µg/day);
- Food (swallowed) - 3 µg/day, and
- Chewing gum (swallowed) - 8 µg/day.
Exposure arising from tobacco smoking is included for comparison:
- Passive smoking of tobacco (inhaled) - 9 µg/day, and
- Heavy smoker (20 cigarettes/day) (inhaled) -</td><td>Adult</td><td>+++</td><td></td></tr>
</table>

				400 µg/day. Sporadic exposures following specific events/activities are as follows: - New carpet (inhaled) - 2 mg/event -Liquid resin (inhaled) - 413 mg/event - Liquid resin (on the skin surface) - 11,000 mg/event - Resin paste (inhaled) - 68 mg/event - Resin paste (on the skin surface) - 5,500 mg/event - Boat building (inhaled) - 4,330 mg/event - Boat building (on the skin surface) - 1640 mg/event. Adult consumer, combined long-term exposure: release of residual styrene monomer from polymeric building materials (80 µg/day), via food (3 µg/day) and from chewing gum (8 µg/day) = total exposure of about 90 µg/day (1.3 µg/kg bw/day)			
			Indirect environmental exposure	No unacceptable human health risk was identified through indirect exposure via the environment and, neither the contributions from drinking water nor food alone are expected to pose a risk to human health.			

Danish EPA-LOUS (2014d)	LOUS survey on white spirit	Contains among others a compilation of data regarding products containing white spirit and direct and indirect exposure of the population	Lacquers/paints (dermal, inh) Cleaning solvents (dermal/inh) Shoe polish	Painting: Various realistic scenarios depending of ventilation, area of treatment: 270 to 6140 mg/m3 Average levels: 470 mg/m3 to 600 mg/m3 Shoe polish: 960 mg/m3 (inhalation); dermal exposure of 192 mg.	adults	+++	
Overall evaluation: The above Danish EPA report serve as a good background for estimating exposure levels for the target population of this project. All of the projects have made use of the data in the Danish EPA database of substances in consumer products. No human biomonitoring studies in Denmark or similar countries weres identified.							

References

Danish EPA 2016a).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

Danish EPA 2016b). Survey and risk assessment for chemicals in rugs for children. Survey of chemical substances in consumer products No.xxx, 2016. Danish Environmental Protection
Agency.

Danish-LOUS (2014a). Survey of n-hexane. Environmental Project No. 1628. Part of the LOUS-review. Danish Environmental Protection Agency.

Danish-LOUS (2014b). Survey of toluene. Environmental Project No. 1613. Part of the LOUS-review. Danish Environmental Protection Agency

Danish-LOUS (2014c). Survey of styrene. Environmental Project No. 1612. Part of the LOUS-review. Danish Environmental Protection Agency.

Danish-LOUS (2014d). Survey of white spirit. Environmental Project No. 1546. Part of the LOUS-review. Danish Environmental Protection Agency.

Lead and substances							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/ total exposure;** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
DTU Food (2015)	Expert evaluation	Lead content in food items were measured in the period of 2004-2011 and based on the consumption pattern of food items of the Danish population the lead intake from food was estimated	Food (oral) highest contribution from Beverages (46%) and Fruit and fruit products (17%)	Total exposure (mean): Children (4-14 years): 0.30 µg/kg/d Adults: 0.23 µg/kg/d Total exposure (95-perc): Children (4-14 years): 0.56 µg/kg/d Adults: 0.41 µg/kg/d 99-perc (whole population): 1,05 µg/kg/d	Children 4-14 years Adults above 14 years Whole population	+++	
Danish EPA-LOUS 2014	LOUS review	Overall compilation of data. Identification of sources and exposure with focus on the Danish population.	Food (oral) Drinking water (oral) Soil (oral) Dust (oral)	For contribution from food the report refers to data from EFSA (2012) and DTU Food (2015 however an earlier version). Drinking water, average: Children 2 years: 0.07 µg/kg/d Drinking water, high level at limit value: Children 2 years: 0.77 µg/kg/d Soil, at quality criteria:	Children 2 years	+++	The report further contains data on health impact assessment of lead exposure to small children (½-3 years) due to mouthing of articles.

			Various lead-containing articles e.g. jewelleries that may be mouthed by small children	Children 2 years: 0.3 µg/kg/d Dust: Children 2 years: 0.6 µg/kg/d Very variable contributions depending of type of articles and the content and migration of lead from the article			
ECHA/RAC 2014	Expert assess-ment	Estimates of exposure of infants and toddlers to lead through mouthing of lead containing objects are given.	Various articles for consumer use that may be mouthed by tod-dlers	Exposure estimates based on mouthing behav-ior: Infants (½-1year) Realistic: 0.01 – 1.5 µg/kg/d Worst-case: 0.06 – 6.2 µg/kg/d Toddlers (1-2 year) Realistic: 0.01 – 1.2 µg/kg/d Worst-case: 0.04 – 4.0 µg/kg/d Toddlers (2-3 year) Realistic: 0.008 – 0.8 µg/kg/d Worst-case: 0.08 – 9.0 µg/kg/d	Infants (½-1year Toddlers (1-2 year) Toddlers (2-3 year)	+++	The report further contains data on health impact assessment of lead exposure to small children (½-3 years) due to mouthing of arti-cles.
EFSA (2012)	Expert	EFSA update of the dietary	Food (oral)	Total dietary exposure (mean):	Various	+++	The report con-

	evaluation	lead exposure to the European population. The exposure estimates was based on more than 144,000 analytical results on lead content in food items coupled with food consumption data of the various age groups in the population.	*For infants and toddlers*: Infant food, drinking water, milk and dairy products, grain products and vegetables were considered most important sources. *For adults:* Beverages, grain products and vegetables were considered most important sources.	Infants: 0.73-1.09 µg/kg/d Toddlers: 0.87-1.18 µg/kg/d Adults: 0.43-0.57 µg/kg/d Total dietary exposure (95-perc.): Infants: 1.39-2.22 µg/kg/d Toddlers: 1.95-2.56 µg/kg/d Adults: 0.74-0.97 µg/kg/d	age groups e.g. Infants Toddlers Adults		cluded that lead content in food and population exposure had shown a decline since the evaluation by EFSA (2010) that was based on older data.
EFSA (2010)	Expert evaluation	Based on data on lead content in food items in EU and consumption pattern of the population as well as based on national surveys the lead intake of various age groups in the EU population was	Food (oral). Infant formula, Cereal products, beverages, vegetables, vegetable products and drinking water	Total dietary exposure (mean): Infants 3 months (infant formula): 0.27-0.63 µg/kg/d Children 1-3 years: 1.10-3.10 µg/kg/d Women 20-40 years: 0.38-1.28 µg/kg/d Total dietary exposure (high level):	Children various age groups Adults	++	Do also contain detailed review on toxicity data, identification of BMDL for various toxic responses and risk characteriza-

		estimated.	were considered most significant sources in EU.	Infants 3 months (infant formula): 0.40-0.94 µg/kg/d Children 1-3 years: 1.71-5.51 µg/kg/d Women 20-40 years: 0.68-2.60 µg/kg/d			tion. Exposure data further updated in EFSA 2012
Selected biomonitoring studies							
Christensen et al (2016)	Human biomonitoring (whole blood)	Lead and cadmium were measured in pregnant women		No exposure calculations.	Pregnant women (n=117), Ukraine and Greenland)	+	Ukraine and Greenland
Hrubá et al (2012)	Human biomonitoring (whole blood)	Lead, mercury and cadmium were measured in children from six European cities, China, Morocco and Ecuador		No exposure calculations	Children 7-11 years old		Sweden, Slovenia, Slovakia, Poland, Czech Republic and Croatia (China, Ecuador and Morocco)
Overall evaluation: The data from Danish EPA (2014), EFSA (2012) and DTU Food (2015) contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. In the Danish database on consumer product many products containing lead are found, however, the clearly highest exposure potential was found from metallic jewelry and for mouthing of this.							

References

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Danish EPA-LOUS (2014). Survey of lead and lead compounds. Environmental Project No. 1539. Part of the LOUS-review. Danish Environmental Protection Agency.

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. edition, june 2015

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Hrubá et al (2012) Blood cadmium, mercury, and lead in children: An international comparison of cities in six European countries, and China, Ecuador, and Morocco. Environment International 41 (2012) 29–34

Mercury and compounds							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
SCENIHR 2015	Expert evaluation	Specifcally addressing exposure from dental amalgam and using EFSA 2012 data on diet exposure as well	Dental amalgam fillings (oral/inhalation)	***Inorganic mercury:*** Adults: 3-17 µg Hg/day (0.05-0.28 µg Hg/kg bw/d	Adults	+++	Contains also biomonitoring data, toxicological information and risk assessment
DTU Food 2015	Expert evaluation	Exposure estimates based on data from Danish food monitoring programme (2004-2011)	Food (oral) 68% of exposure from fish products	***Methylmercury:*** 4-74 years (mean): 0.018 µg/kg bw/d 4-74 years (95-perc): 0.051 µg/kg bw/d ***Inorganic mercury:*** 4-74 years (mean): 0.012 µg/kg bw/d 4-74 years (95-perc): 0.034 µg/kg bw/d	Population estimate 4-75 years	+++	Contains risk assessment as well.
Danish EPA 2014	LOUS survey	Refer to data from RFSA 2012 and from the Danish Food monitoring programme	Food (oral) Dental amalgam	Refer to data also presented by DTU Food (2015) and EFSA (2012)	Population exposure	++	
EFSA 2012	Expert evaluation	Assessing dietary exposure to either methylmercury or inorganic mercury for various age groups based on data of the content in food items and	Food (oral)	***Methylmercury:*** Total exposure (median values of average exposure values): Toddlers: 0.09 – 1.57 µg Hg/kg/week Adults: 0.07 – 1.08 µg Hg/kg/week	Adults Toddlers and various other age groups	+++	Contains also biomonitoring data, toxicological information and risk as-

		the consumption pattern of the various food items.		Total exposure (median values of 95-percentile values): Toddlers: 0.68 – 2.72 µg Hg/kg/week Adults: 0.51 – 3.04 µg Hg/kg/week ***Inorganic mercury:*** Total exposure (median values of average exposure values): Toddlers: 0.79 – 1.36 µg Hg/kg/week Adults: 0.39 – 0.73 µg Hg/kg/week Total exposure (median values of 95-percentile values): Toddlers: 1.35 – 2.30 µg Hg/kg/week Adults: 0.53 – 1.66 µg Hg/kg/week			sessment
SCHER 2010	Expert evaluation	Exposure estimates are based on measurements of Hg in air in connection with a broken energy-saving light bulb containing mercury	From broken energy-saving light bulb (inhalation)	7-year old child: Scenario without venting: 10 µg/kg bw for 2 days Scenario with immediate venting: 0.6 µg/kg bw/d for one day	7-year old child	+++	Contains risk assessment as well
Selected biomonitoring studies							
Mørck et al (2015)	Research study	Human biomonitoring in DK	-	The intake of fish was significantly associated mercury concentrations in hair. No exposure calculations. Concentrations in µg/g hair	Children 6-11 years and their	+	No exposure calculation

					mothers (n=145 pairs)		
Castaño et al (2015)	Research study	Human biomonitoring in 17 countries in EU	-	The intake of fish was significantly associated mercury concentrations in hair. No exposure calculations. Concentrations in µg/g hair	Children 6-11 years and women	+	No exposure calculation
Golding et al (2012)	Research study	Human biomonitoring in UK (ALSPAC cohort)	-	Dietary components associated with mercury level in blood were seafood, but also herbal tea and wine. No exposure calculations	Pregnant women (n=4484)		No exposure calculations
Hrubá et al (2012)	Human biomonitoring (whole blood)	Lead, mercury and Cadmium was measured in children from six European cities, , China, Morocco and Ecuador		No exposure calculations	Children 7-11 years old		Sweden, Slovenia, Slovakia, Poland, Czech Republic and Croatia (China, Ecuador and Morocco)
Overall evaluation: The data from SCENIHR (2015), EFSA (2012) and DTU Food (2015) contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. For exposure from damaged energy-saving light bulbs data from SCHER (2010) is considered relevant. In the Danish database on consumer only very few products containing mercury are found. The data indicate that an exposure potential may come from jewelry containing mercury.							

References

Castaño et al (2015) Fish consumption patterns and hair mercury levels in children and their mothers in 17 EU countries. Environmental Research 141 (2015) 58-68

Danish EPA-LOUS (2014). Survey of mercury and mercury compounds. Environmental Project No. 1544. Part of the LOUS-review. Danish Environmental Protection Agency.

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. edition, june 2015

EFSA (2012). Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal 2012;10(12):2985

Golding J, Steer CD, Hibbeln JR, Emmett PM, Lowery T, Jones R. 2013. Dietary predictors of maternal prenatal blood mercury levels in the ALSPAC birth cohort study. Environ Health Perspect 121:1214–1218

Hrubá et al (2012) Blood cadmium, mercury, and lead in children: An international comparison of cities in six European countries, and China, Ecuador, and Morocco. Environment International 41 (2012) 29–34

Mørck et al (2015) The Danish contribution to the European DEMOCOPHES project: A description of cadmium, cotinine and mercury levels in Danish mother-child pairs and the perspectives of supplementary sampling and measurements. Environmental Research 141 (2015) 96–105

SCENIHR (2015). SCENIHR Opinion on The safety of dental amalgam and alternative dental restoration. Scientific Committee on Emerging and Newly Identified Health Risks. The

SCENIHR adopted this opinion at the 10th plenary meeting on 29 April 2015.

SCHER (2010). Opinion on Mercury in certain Energy-saving Light Bulbs – Exposure of Children Scientific Committee on Health and Environmental Risks. The SCHER adopted this opinion at its 16th plenary on 22 March 2012

Nonylphenol							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST-LOUS 2013	Danish EPA report	Survey on exposure to alkylphenols and -epoxylates		Limited information on nonylphenol applications, no calculated data on exposure		+	
MST 2012a	Danish EPA report	Data from other sources (food: EU Risk assessment report; Us data for dust and air; measured values for clothes)	Food (oral) Dust (oral) Air (inh) Clothes (dermal)	High (and mean): 0.2 ug/kg bw/day (EU RAR 2002) Mean and high: 0.0002 and 0.0002 ug/kg bw/day Mean and high: 0.03 and 0.11 ug/kg bw/day Mean and high: 4.5 and 9.1 ug/kg w/day	Adult	+++	US data for dust and indoor air. Conservative approach
MST 2012b	Danish EPA report	Literature based and measured values of nonylphenol in textiles	Clothes (dermal)			++	Data from this report used for exposure assessment in MST 2012a
Gyllenhammar 2012	Research paper	Calculated intake from foods (and biomonitoring data without exposure calculations)	Food (oral)	Mean 27.2 ug/day (range 14-40) = 0.45 ug/kg bw/day	Nursing women	+++	Sweden

MST database	Danish EPA reports	Surveys and chemical analysis in selected products		In the Danish database on consumer products a few other reports on products containing nonylphenol are found, but these were not considered relevant		+/+++	Window paints, sex toys, artificial grass
ECB 2002	Expert evaluation (EU RAR)	Upper limit of food intake of nonylphenol	Food (oral)	High (upper limit): 0.2 ug/kg bw/day	Adult	+++	10% bioavailability
Selected biomonitoring studies							
Pirard 2012	Research paper	Biomonitoring, nonylphenol, BPA, triclosan		No exposure estimates	Adult, children	+	Belgium. Lack of calculated exposure
Asimakopoulos 2012	Research paper	Biomonitoring review, nonylphenol and BPA		No exposure estimates	Adult, children	+	Lack of calculated exposure
Overall evaluation: The data from MST 2012a contain data considered sufficient for making exposure estimates for pregnant women in this project. Data for children are lacking.							

References:

Asimakopoulos AG, Thomaidis NS, Koupparis MA. Recent trends in biomonitoring of bisphenol A, 4-t-octylphenol, and 4-nonylphenol. Toxicol Lett. 2012 Apr 25;210(2):141-54.

ECB 2002. EU Risk assessment report. 4-Nonylphenol (branched) and nonylphenol. CAS Nos: 84852-15-3 and 25154-52-3.

Gyllenhammar I, Glynn A, Darnerud PO, Lignell S, van Delft R, Aune M. 4-Nonylphenol and bisphenol A in Swedish food and exposure in Swedish nursing women. Environ Int. 2012 Aug;43:21-8.

MST 2012a: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer

MST 2012b: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 120, 2013. Kortlægning samt miljø- og sundhedsmæssig vurdering af nonylphenol og nonylphenolethoxylater i tekstiler

MST-LOUS 2013: Survey of alkylphenols and alkylphenol ethoxylates. Part of the LOUS-review. Environmental project No. 1470, 2013.

Pirard C, Sagot C, Deville M, Dubois N, Charlier C. Urinary levels of bisphenol A, triclosan and 4-nonylphenol in a general Belgian population. Environ Int. 2012 Nov 1;48:78-83.

Organophosphate flame retardants **Trichloroethyl phospshate (TCEP), Tricresyl phosphate (TCP) and dicresylphenyl phosphate**							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/total exposure;** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Langer et al (2016)	Scientific research paper	Measurements of organophosphate flame retardants in dust samples from Danish homes and daycare centers	Dust (oral and inhalation)	No exposure calculations but serum measurements in µg/g dust	Various age groups; households and daycare centers	++	Danish paper also includes review table of previous published data on the dust samples
Danish EPA (2015)	Study report	Assessment and calculation of children's exposure to chemicals from applying used material in creative activities	Re-used materials (oral, dermal and inhalation)	Results for tricresyl phosphate and Dicresylphenyl phosphate: The migration rate was not measured but at calculated migration rates above 1.8 µg/cm2/hour from the material the RCR > 1 for dermal exposure.	Children	+/++	
Danish EPA (2015b)	Study report	Assessment and calculation of children's exposure to chemicals based on survey and analysis of chemicals in car safety seats	Car seats (dermal and oral)	Daily dermal and oral exposure to TCEP is calculated for each car seat	Children aged 1-12 months	+++	RCR for some of the car safety seats analysed is > 1

Hoffmann et al (2015)	Scientific paper	Measurements of organo-phosphate flame retardants in hand wipes and dust samples from adult volunteers in North Carolina US	Dust (oral)	No exposure calculations but measurements in ng/g	Adults House-holds	+	US study
SCHER (2012)	Expert opinion	Exposure and risk evaluation on tris(2-chloroethyl)phosphate (TCEP) is made from a re-view of existing data on the subject	Dust intake (oral, inhalation) Air (inhalation) Toys (oral, der-mal) Furniture (dermal)	Total daily exposure in children 1-3 years old: 13.19-13.79 µg/kg bw/day	Small children 1-3 years old	+++	
ARCADIS (2011)	Expert report	Evaluation of human expo-sure and risk assessment to chemicals including organo-phosphate flame retardants	Emission from products such as wood impregna-tion, carpets, glues, plastics etc.	TCEP: Results from EU-RAR (2009) used: Female adults: 4.5 µg/kg bw/day Children 1-3 years: 11 µg/kg bw/day Baby 3 months: up to 240 µg/kg bw/day	Various age groups; Infants, children, adults	+++	

			Dust intake (oral, inhalation) Air (inhalation, dermal) Toys (oral)	TCP: External exposure estimates are given from Wire and cable: Inhalation: 5.29 µg /m^3 (SVC) Furniture: Inhalation: 5.29 µg /m^3 (SVC) 21 ng/m^3 (airborne particulates) Dermal: 36.5 mg/kg bw/day Cresyl diphenyl phosphate: External exposure estimates are given from Wire and cable: Inhalation: 4.61 µg /m^3 (SVC) Furniture: Inhalation: 54.61 µg /m^3 (SVC) 125 mg/m^3 (including vapour and airborne particulates) Dermal: 36.5 mg/kg bw/day			
EU-RAR (2009)	Expert risk assess-ment	Exposure and risk evaluation on tris(2-chloroethyl)phosphate (TCEP)	Emission from products such as wood impregna-tion, carpets, glues, plastics etc.	Total daily exposure (worst case): Female adults: 4.5 µg/kg bw/day Children 1-3 years: 11 µg/kg bw/day Baby 3 months: up to 240 µg/kg bw/day	Various age groups; Infants, children, adults	+++	

			Dust intake (oral, inhalation) Air (inhalation, dermal) Toys (oral)				
Selected biomonitoring studies							
Kucharska et al (2015)	Scientific paper	Human biomonitoring study of organophosphate flame retardants in a Norwegian mother–child cohort	All	No exposure calculations but measurements in hair and urine	Adults (women) and children aged 6-12 years	+	Norway
Overall evaluation: The data from EU-RAR (2009), SCHER (2012), ARCADIS (2011) and EPA data on consumer product materials contain updated data of high quality and the data are considered sufficient for making exposure estimates for TCEP. In the Danish database on consumer products TCEP has been found in several consumer products including toys and products for infants and young children. The primary exposure sources for children are through intake of dust, hand-to-mouth exposure and playing with toys containing organophosphate flame retardants, including for small children sucking on items. It is concluded that sufficient data on the compound TCEP is available and thus this compound is taken further for a more detailed exposure assessment and risk assessment.							

References

ARCADIS (2011). Contract number 17.020200/09/549040. Identification and evaluation of data on flame retardants in consumer products P3-402

Danish EPA (2015). Chemical substances in car safety seats and other textile products for children. Survey of chemical substances in consumer products No. 135, 2015

Danish EPA (2015b). Børneinstitutioners anvendelse af materialer fra brugte produkter. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 143, 2015. Danish Environmental Agency

EU-RAR (2009). European Union Risk Assessment Report on TRIS (2-CHLOROETHYL) PHOSPHATE, TCEP, July 2009, p 1-213

Hoffmann et al (2015). Monitoring indoor exposure to organophosphate flame retardants: hand wipes and house dust. Environ Health Perspect 123:160–165

Kucharska et al (2015). Assessment of human hair as an indicator of exposure to organophosphate flame retardants. Case study on a Norwegian mother–child cohort. Environment International 83:50–57

Langer et al (2016). Organophosphate esters in dust samples collected from Danish homes and daycare centers. Chemosphere, 154:559-566.

SCHER (2012). SCHER (Scientific Committee on Health and Environmental Risks), Opinion on tris(2-chloroethyl)phosphate TCEP in Toys, 22 March 2012.

Propyl- and Butylparaben							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST 2014	Danish EPA report	Survey of preservatives in toys (modelling clay, face paint, hobby paint)	Products	Butyl- and propylparaben detected in slime products, and not in modelling clay, face paint and other products	Children	++	Calculations of worst case exposure from several products (not based on chemical analysis)
MST LOUS 2013	Danish EPA report	Survey of literature on parabens	Products	No calculated exposure		+	Lack of calculated exposure with reference to lack of optimal methods of exposure estimation by authorities
SCCS 2013	Expert evaluation	Conservative approach combining maximal exposure values and maximum permitted levels		High: Systemic exposure dose adult: 20 ug/kg bw/day (with new lower maximum limit) Systemic exposure dose children: (0.0008+0.0076+0.0001+0.0003=0.0088 mg/kg) =10 ug/kg bw/day excluding use in nappy area (not recommended)	Adult, children 3 months	+++	Sum of propyl- and butyl paraben
MST 2012	Danish	Literature based calculation	Cosmetics, air	Mean: 2-3 ug/kg bw/day x2	Adult	+++	”Pregnant con-

	EPA report	of exposure from cosmetics, dust and air		High: 18 ug/kg bw/day x2 Sunscreen: 11 or 88 ug/kg bw/day x2	women		sumers project". Sum of propyl- and butyl paraben
MST 2009	Danish EPA report	Survey and chemical analysis in selected products	Products	Detection of propylparaben in several lotions and sunlotions, detection of butylparaben in one lotion and one sunlotion. It is concluded that face paint, make up and lipgloss will only make a minor contribution to exposure to these parabens	2-year olds	+++	Overview of data in several EPA surveys from 2002-2009
MST 2002-2009	Danish EPA reports	Surveys and chemical analysis in selected products	Products	In the Danish database on consumer product many products containing propyl- and butylparaben are found, and several products may be relevant to children and possibly the unborn child.		+/+++	Some reports may include exposure assessment. Some data are included in project on 2-year olds and pregnant consumers
MST 2006	Danish EPA report	Survey and chemical analysis in selected products	Products	Propylparaben detected in several slime products; butylparaben detected in one glue/paint. Considered to be in low concentrations of low risk	Children	+	Lack of calculated exposure.
Selected biomonitoring studies							
Fernandez 2016	Research study	Placenta measurement		No exposure estimates	Placenta	-	Lack of exposure calculations
Myridakis 2016	Research study	Biomonitoring		Calculated intake (see paper for exact values)	Preschool children	+	Greece
Dewalque	Research	Biomonitoring		No exposure estimates	Children,	+	Lack of exposure

2014	study				women		calculations. BE data 2013
Myridakis 2015	Research study	Biomonitoring		Calculated intake (see paper for exact values)	Mothers, children	+	Greece
Frederiksen 2014	Research study	Overview of biomonitoring data 2006-2012		No exposure estimates	Children, women	+	Lack of exposure calculations
Larsson 2014	Research study	Biomonitoring, Sweden, Parabens, phthalates, bpa, triclosan		No calculation of exposure, but urinary concentrations	Adult women, children 6-11 years	+	Lack of calculated exposure
Moos 2014	Research study	Biomonitoring		No exposure estimates	Children, adults	+	Lack of exposure calculations
Gosens 2014	Research study	Aggregate exposure modelling based on data for product use		Internal exposure estimates are presented graphically as probability of intake. These data may be useful for extracting information on mean and high exposure estimates for children	Children 0-3 years	+++	NL study on data on product use
Frederiksen 2013	Research study	Biomonitoring, Denmark, Parabens, phthalates, bpa		No calculation of exposure, but urinary concentrations	Adult women, children 6-11 years	+	Lack of calculated exposure
Schlumpf 2010	Research study	Biomonitoring		Exposure estimates for intake by infants	Infants/milk	++	CH 2004-2006
Overall evaluation: The data from MST 2012 and SCCS 2013 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. In the Danish database on consumer product products containing butyl- and propylparaben are found, however, the highest exposure potential was found from propylparaben in cosmetic products. Literature search is limited to recent Danish biomonitoring data and to child-specific European data.							

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MST LOUS 2013: Survey of parabens. Part of the LOUS-review. Environmental Project No. 1474, 2013
MST 2014: Forbrugerprodukter nr. 123, 2014. Kortlægning og sundhedsmæssig vurdering af konserveringsmidler i legetøj
MST 2002-2009: Several publications including: Kortlægning af kemiske stoffer i forbrugerprodukter, 58, 2005: Kortlægning af kemiske stoffer i tekstilfarver. Kortlægning af kemiske stoffer i forbrugerprodukter 5, 2002: Kortlægning af kemiske stoffer i fastelavns- og teatersminke. Kortlægning af kemiske stoffer i forbrugerprodukter 2006: Kortlægning og sundhedsmæssig vurdering af kemiske stoffer i sexcreme (pleasure gel). Kortlægning af kemiske stoffer i forbrugerprodukter, 69, 2006: Kortlægning og sundheds- og miljømæssig vurdering af håndsæbe. Kortlægning af kemiske stoffer i forbrugerprodukter, 67, 2006: Kortlægning og afgivelse af kemiske stoffer i "slimet" legetøj. Kortlægning af kemiske stoffer i forbrugerprodukter, 105, 2009: Kortlægning og sundhedsmæssig vurdering af produkter til indvendig bilpleje. Kortlægning af kemiske stoffer i forbrugerprodukter, 59, 2005: Kortlægning og vurdering af kemiske stoffer i glas- og porcelænsfarver. Kortlægning af kemiske stoffer i forbrugerprodukter 44, 2004: Kortlægning af kemiske stoffer i dyreplejeprodukter.
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Paracetamol							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Magnus 2016	Research paper	Questionnaire on use of paracetamol during pregnancy and in infants	Medicine (oral/rectal)	27.9% of children were exposed to paracetamol during pregnancy, 15.5% during infancy and 19.1% were exposed both during pregnancy and infancy	Pregnant women and infants	++	Norway
Ersboll 2015	Research paper	Questionnaire on use of paracetamol before and during early pregnancy	Medicine (oral)	0.2 % of pregnant women used paracetamol daily 0.7% of pregnant women used paracetamol 1-2 times per week	Pregnant women	++	Denmark
Liew 2015	Research paper	Questionnaire on use of paracetamol during pregnancy	Medicine (oral)	More than 50% of women used paracetamol during pregnancy	Pregnant women	++	Denmark
Ermann 2012	Research paper	Diary study on use of paracetamol in children	Medicine (oral/rectal)	65% of toddlers received paracetamol during a 3 months period. 10% of toddlers received paracetamol for more than 10 days	Toddlers 11-14 months of age	++	Denmark
Selected biomonitoring studies							
Nielsen 2015	Research paper	Biomonitoring	Medicine and other	Biomarkers of paracetamol use in all children and mothers. No data on exposure frequency.	Mothers and children	+	Denmark concluded that other sources of exposure than medical

							use may occur
Overall evaluation: Several papers investigate the use of paracetamol in children and pregnant women. Only recent studies from Denmark/Scandinavia are included here. These data are considered sufficient for making exposure estimates for this project.							

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<table>
<tr><th colspan="8">PCB /TCDD</th></tr>
<tr><th>Reference</th><th>Type of study</th><th>Method/content</th><th>Exposure sources;
(exposure routes)</th><th>Exposure contribution from specific sources/total exposure;
(mean-typical/high)</th><th>Target groups</th><th>Relevance for exposure assessment in this project</th><th>Comments</th></tr>
<tr><td>DTU Food (2015)</td><td>Expert evaluation</td><td>PCB content in food items were measured in the period of 2004-2011 and based on the consumption pattern of food items of the Danish population the lead intake from food was estimated</td><td>Food (oral)</td><td>For dioxins andDL-PCBs as well as for 6 or 10 indicator PCBs the following intake estimates for the Danish population were derived:
<table>
<tr><th></th><th colspan="2">WHO-TEQ2005 Dioxins+PCB pg/kg bw/day</th><th colspan="2">PCB-6 ng/kg bw/day</th><th colspan="2">PCB-10 ng/kg bw/day</th></tr>
<tr><td>TDI</td><td colspan="2">2</td><td colspan="2">10</td><td colspan="2">20</td></tr>
<tr><td>Mean</td><td>0.55</td><td>0.87</td><td>1.8</td><td>2.7</td><td>5.7</td><td>8.9</td></tr>
<tr><td>Percentiles</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>50</td><td>0.46</td><td>0.73</td><td>1.5</td><td>2.1</td><td>4.7</td><td>7.5</td></tr>
<tr><td>95</td><td>1.2</td><td>1.9</td><td>4.3</td><td>6.3</td><td>12.7</td><td>20.4</td></tr>
<tr><td>99</td><td>2.0</td><td>2.6</td><td>7.1</td><td>9.4</td><td>21.4</td><td>28.4</td></tr>
<tr><td>Max</td><td>3.4</td><td>3.4</td><td>16.4</td><td>12.5</td><td>41.0</td><td>41.0</td></tr>
<tr><td>Population (year)</td><td>4-75</td><td>4-14</td><td>4-75</td><td>4-14</td><td>4-75</td><td>4-14</td></tr>
</table></td><td>Children 4-14 years
Adults above 14 years
Whole population</td><td>+++</td><td></td></tr>
<tr><td>Danish EPA (2014)</td><td>Danish background documentation for deriving limit value of PCB in soil</td><td>Exposure estimate is based on review of literature data. Specific estimates based on analysed PCB levels in food items and consumption data on food items</td><td>Food (oral)</td><td>Average exposure:
10 specific indicator PCBs: 0.04-0.10 µg/d (0.9 µg/d PCB_{sum10})
95-percentile exposure:
10 specific indicator PCBs: 0.07-0.21 µg/d (1.66 µg/d PCB_{sum10})</td><td>Population 15-75 years</td><td>++</td><td>The report also includes risk characterisation. DTU (2015) contains updated exposure estimates</td></tr>
</table>

Danish HMA (2013)	Study report	Review on PCB in Danish indoor environment. Exposure related mostly to serum levels and only sparse data on actual exposure estimates.	Building materials (inhalation and oral)	**Inhalation, 6 indicator PCBs (300-3 000 ng PCB_6/m3)** Adult: 6 000-60 000 ng PCB_6/ d	Population	++	Contain toxicological evaluation as well.
Danish HMA (2012)	Study report	PCB levels were measured in indoor air in apartments with PCB sealings and compared to PCB plasma levels of the inhabitants,	Building materials (inhalation and oral)	The exposed dwellers had about 4-folds higher blood-PCB concentrations than the non-exposed: The longer the residence time, the higher the blood concentration of low-chlorinated PCBs. No specific exposure estimates were made.	Adults	+++ *Exposure estimates can be made from the PCB levels found in indoor air.*	
EFSA (2012)	Expert evaluation	Based on analytical data of the content of PCB and dioxins in food items in EU in the period of 2008 to 2010 and based on food consumption data, estimates of the exposure of the EU population were made for various age groups.	Food (oral)	**Total diet exposure to dioxins + DL PCBs, (in pg TCDD eqv/ kg bw/d)** mean / 95 perct Infants 1.08 – 1.17 / 3.0 – 5.9 Toddlers 1.54 -2.54 / 2.6 – 9.9 Adults 0.57 – 1.64 / 1.9 – 4.5 Danish popul. 1.06 / 2.3 **Total diet exposure to NDL PCBs, (in ng / kg bw/d)** mean / 95 perct Infants 7.2 – 11.0 / 17.7 – 35.4 Toddlers 8.3 – 25.7 / 18.2 – 52.7	Infants. Toddlers, Adults and other age-groups	+++	

				Adults 3.8 – 11.5 8.1 – 33.0 Danish popul. 5.4 - 6.3 10.8 – 11.8			
Danish EPA (2009)	Study Report	PCB levels were measured in indoor environment in homes public buildings and exposure estimates were performed based on measured data	Building materials (inhalation; oral for dust and soil)	**Inhalation, NDL PCBs (1 µg PCB/m^3 in air)** Children (1-5 years): 0.5 µg/kg bw/d **Oral, dust (2 µg PCB/ g**) Children (1-3 years): 8 ng /kg bw/d **Oral, soil (350 ng PCB/g)** Children (1-3 years): 2.7 ng /kg bw/d	Children 1-5 years	+++	Includes toxicological evaluation and risk assessment
Frederiksen et al (2012)	Research paper	Measurements of indoor air and sealants contaminated with PCB	Building material (inhalation)	No exposure calculations but levels in ng/m^3 air and mg/kg sealant Indoor air concentrations were reduced in homes where people reported to clean and airing more frequently	83 air samples and 20 sealants (contaminated) and 20 21 reference apartments	++	DK buildings
Harrad et al. (2006)	Research paper	PCB levels were measured in indoor air UK in and exposure estimates were made for toddlers and adults	Building materials (inhalation)	**Inhalation, total PCB ng/d** Median 95-perct Toddlers 11 111 Adults 60 586	Toddlers Adults	+++	
Selected biomonitoring studies							
Lignell et al (2016)	Research paper	Human biomonitoring in human breast milk (PCB 28 and PCB 153)	Breast feeding (oral)	Infant daily intake of PCB 28 and PCB 153 was calculated 8-12 weeks post partum: PCB 28: 5.4 ± 2.6 (1.8-14) ng/kg bw/day PCB 153: 147 ± 74 (67-297) ng/kg bw/day	Infants 8-12 weeks and 20-24 weeks	++	Sweden

				For calculations for 20-24 weeks see reference	(n=68)		
Mørck et al (2014)	Research paper	Human biomonitoring of PCBs and dioxin-like activity	-	No exposure calculations	Children 6-11 years of age and their mothers (n=259)	+	Denmark
Meyer et al (2013)	Research paper	Human biomonitoring PCB levels were investigated in plasma from exposed and not exposed residents of a housing estate. Indoor air samples were also taken	Building material (inhalation)	No exposure calculations, but significant association between air and plasma levels of PCBs and 4 times higher PCB levels in exposed individuals	104 flats, 134 exposed and 139 non-exposed individuals	+	Denmark
Overall evaluation: Data on dietary exposure to dioxins and PCB is considered sufficiently covered by DTU Food (2015) and EFSA (2012). Data on PCB exposure from building materials, dust and soil is considered sufficiently covered by Harrad et al (2006) (indoor air), Danish EPA (2009) (indoor air, dust soil) and Danish HMA (2012) (indoor air levels). No additional sources for exposure to dioxins and PCBs are considered relevant for this project.							

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Frederiksen et al (2012) Polychlorinated biphenyls (PCBs) in indoor air originating from sealants in contaminated and uncontaminated apartments within the same housing estate Chemosphere 89 (2012) 473–479

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Lignell et al (2016) Environmental organic pollutants in human milk before and after weight loss. Chemosphere 159 (2016) 96-102

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Mørck et al (2014) PCB Concentrations and Dioxin-like Activity in Blood Samples from Danish School Children and Their Mothers living in Urbanand Rural Areas. Basic & Clinical Pharmacology & Toxicology, 2014, 115, 134–144

Pesticides – all							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Jensen 2015	Research paper	Calculated exposure from foods based on residue concentration measurements and consumption data. Intake estimates are listed for the pesticides with the highest intake relative to acceptable daily intakes (ADIs).	Food (oral)	Intake from food, adults (ug/kg bw/day): Diazinon 0.0047 neurotox) Pirimiphos-methyl 0.043 (MST gravid) Dicofol (sum) 0.017 Procymidone 0.018 (MST gravid) Dimethoate 0.0063 (, neurotox) Carbaryl 0.043 Chlorfenvinphos 0.0028 (neurotox, no reprotox) Carbendazim and benomyl 0.087 neurotox) Dithiocarbamates 0.21 (MST gravid) Linuron 0.010 (neurotox) Methomyl and thiodicarb 0.0083 (neurotox, no reprotox/ED) Methamidophos 0.0029 (neurotox, no reprotox/ED) Imazalil 0.072 (MST gravid) Oxydemeton-methyl (sum) 0.00074 (neurotox)	Adult	+++	Danish data, thus, especially relevant for this project
MST 2012	Danish EPA report	Collection of data mainly from Danish Veterinary and Food Administration 2009 listing the 20 pesticides with	Food (oral) (for chlorpyrifos also dust and air)	Pirimiphos-methyl Procymidone Dithiocarbamates (group) Imazalil	Adult	+++	Pregnant consumers report, slightly older data than presented by

		the highest intake (mean and high (=2x mean) intake). For Procymidone and Tebuconazole probabilistic methods are used (mean and 95th percentile).		Chlorpyrifos Iprodion Propamocarb Tebuconazol Thiabendazol (see report for exact data)			Jensen 2015
Boon 2015	Research paper	European data on residue concentration measurements and consumption data are applied for probabilistic estimates of pesticide intake.		Triazole compounds (top 3 for Denmark includes bitertanol) 99.9 percentile exposure data are listed for adults and adolescents.	Adult, adolescent	+	Lack of exposure data for individual compounds
Selected biomonitoring studies							
EPA (2015)	HBM study	Human biomonitoring of organophosphate metabolites		No calculated exposures	Children 6-11 years old and their mothers	+	DK study
Roca 2014	Research paper	Biomonitoring, school children		No calculated exposure estimates, but urinary measures (ug per g creatinine. Metabolites of chlorpyrifos and diazinon were found	Children	+	Spain. Lack of calculated exposure
Overall evaluation: The data from MST 2012 and Jensen 2015 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. Calculations for children are not currently available. Search for biomonitoring data was limited to recent Danish and European exposure data for children and excluding occupational exposures, and no/few appropriate biomonitoring data were found for these pesticides (metabolites). Data using duplicate diet method were only found for US children. No literature search on pesticide content in dust and indoor air was performed (some US data appeared in a general search, but was not included here). Further refinement of searches may be possible, but were not carried out at this stage. If any of the pesticides turn out to contribute markedly to the cumulative risk assessment it may be relevant to perform further searches for these particular compounds.							

References:

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Jensen BH, Petersen A, Nielsen E, Christensen T, Poulsen ME, Andersen JH. Cumulative dietary exposure of the population of Denmark to pesticides. Food Chem Toxicol. 2015 Sep;83:300-7.

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Roca M, Miralles-Marco A, Ferré J, Pérez R, Yusà V. Biomonitoring exposure assessment to contemporary pesticides in a school children population of Spain. Environ Res. 2014 May;131:77-85.

EPA (2016) Organophosphate metabolites in urine samples from Danish children and women

PFOA; PFOS; PFHxS (belonging to the group of perfluoroalkyl carboxylic acids/ sulfonic acids)							
Reference	**Type of study**	**Method/content**	**Exposure sources;** (exposure routes)	**Exposure contribution from specific sources/total exposure;** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
Danish EPA (2016)	Study report on PFAS in children´s carpets	Carpets for children´s room were analysed for PFAS and exposure estimates and risk assessment was conducted	Carpets (dust (oral))) Content in carpets: PFOS 1,01 ng/g PFOA 5,9 ng/g PFHxS 0,22 ng/g	Exposure PFOA PFOS Children 2 years (ng/kg bw/d) 0.05 0.009	children	+++ Negligible exposure from children´s carpets	In the risk assessment a RCR value of 0.0008 was calculated for the sum of PFOS and PFOA
DTU Food (2015)	Expert evaluation	Based on Danish measurements in fish in 2011 an intake estimate was made for PFOS	Food (oral)	**PFOS** Adult: 27 ng/d or 0.45 ng/kg bw/d	Adult	+++	
Danish EPA (2015a)	Background report for health based quality criteria	Review of expert assessment on PFOA; PFOSA and PFOSA. With regard to exposure presenting the latest exposure estimates	Food (oral)	Refer to data from EFSA (2012) and Danish EPA (2013)	Adults and toddlers	++	
Danish EPA (2015b)	Study report on PFAS in children´s cloth	Measurements of polyfluoroalkyl (PFAS) substances in childrens clothes and assessing exposure of the total exposure of the substances	Clothes (oral, dermal, inhalation)	From clothes Children (4 years): 0.55 ng/ kg bw/d (as total PFAS) However the highest contribution was from 10:2FTPOH and in **general** the content of	Children (4 years)	+++ (indicating negligible exposure from PFOA;	Also risk assessment including, indicating worst case RCR of 0.003 – 0.008.

		and the contribution from the clothes.		PFOA (the major compounds among PFOA; PFOS; PFHxS) was around 1% of the PFAS content.		PFOS; PFHxS)	(DNEL for PFOA used as a surrogate for the total sum of PFAS). Overall the contribution from PFOA; PFOS; PFHxS to this low RCR is considered to be negligible
ECHA/RAC (2015)	Expert assessment	Background document for restriction of PFOA. Exposure estimates for children and adults were made for PFOA	Breast milk (oral) Total exposure (oral) Point towards drinking water and indoor dust as potential for significant exposure (no specific figures given)	Breast fed infant: 4.3 ng PFOA/kg bw/day ***Total exposure estimate, intermediate/median scenario*** **Adults**: the intakes of PFOA are in the range 0.26 to 6.1 ng/kg bw/day **Children ≥ 2years** and teens: the intakes of PFOA are in the range 2.6 to 20.1 ng/kg bw/day **Children < 2 years**: the intakes of PFOA are in the range 4.3 to 9.8 ng/kg bw/day ***Total exposure estimate, high scenario (e.g. high drinking water concentration, high dust concentrations)*** **Adults**: the intakes of PFOA are in the range 4.1 to 44 ng/kg bw/day **Children ≥ 2years** and teens: the intakes of	Infantes children Adult	+++	Contains also DNEL derivation and risk assessment

<table>
<tr><td></td><td></td><td></td><td></td><td>PFOA are in the range 53 to 72 ng/kg bw/day
Children < 2 years: the intakes of PFOA are in the range 83 to 114 ng/kg bw/day</td><td></td><td></td><td></td></tr>
<tr><td>Danish EPA-LOUS (2013)</td><td>LOUS survey</td><td>Review and overall evaluation of PFOA; PFOS and other PFAS.
Collection exposure data as well</td><td>Food
Food packing material
Anti-stick cookware
Clothes
Carpets
Indoor env
(various exp routes)</td><td>Exposure data from food from EFSA (2008).
No data
Insignificant from cookware
Insignificant from clothes
Carpets may be a significant source to children
Dust may be a significant source

Estimated adult daily intake (pg/kg bw/d)<table><tr><th></th><th colspan="2">PFOS</th><th colspan="2">PFOA</th></tr><tr><th></th><th>Mean</th><th>High</th><th>Mean</th><th>High</th></tr><tr><td>Indoor air</td><td>0.9</td><td>0.9</td><td>4.7</td><td>4.7</td></tr><tr><td>Outdoor air</td><td>1.3</td><td>12.0</td><td>0.1</td><td>1.0</td></tr><tr><td>House dust</td><td>16.4</td><td>1,028.3</td><td>31.7</td><td>4216.7</td></tr><tr><td>Diet</td><td>2,816.7</td><td>11,483.3</td><td>1,500.0</td><td>4,483.3</td></tr><tr><td>Drinking water</td><td>21.7</td><td>86.7</td><td>23.3</td><td>130.0</td></tr><tr><td>Overall intake</td><td>2,857</td><td>12,611</td><td>1,560</td><td>8,836</td></tr></table></td><td>Adults
Children</td><td>Food + (not up to date)

Indoor +++</td><td>Food-contact material may be considered as probably relevant source</td></tr>
<tr><td>Livsmedelsverket (2013)</td><td>Expert evaluation</td><td>Based on analytical data from Sweden and based on food consumption pattern exposure estimates for PFOA, PFOS and other PFAS were made.</td><td>Food (oral)</td><td>PFOS exposure (ng/d)

Median
95-perct
Children 2 years 15.2
39.3
Women (18-45 years) 22.2
68.9</td><td>Children 2 years
Women 18-42 years and other age groups</td><td>+++</td><td></td></tr>
</table>

				PFOA exposure (ng/d) **Median** **95-perct** Children 2 years 37.8 56.1 Women (18-45 years) 34.1 51.5 **PFHxS exposure (ng/d)** **Median** **95-perct** Children 2 years 1.87 2.77 Women (18-45 years) 1.91 2.86			
NCM (2013)	Project report	Review on PFAS occurrence, exposure, toxicology and risks. Exposure estimates based on measured data and intake rates.	Food (oral) Drinking water Indoor env. Food packing Coating Carpet sprays	Exposure on PFOS, PFOA and PFHxS from diet comparable to Swedish figures, however, not divided in subgroups according to age. Contaminated drinking water, food packing materials and coatings and carpet sprays considered as important sources. **Indoor env:** **PFOS (ng/kg bw/d)** Average exposure, dust: 0.11-0.46 Average exposure, air: 0.004-0.36	Adults	+++	Food packing material and coatings and carpet sprays considered as potential significant sources

				PFOA (ng/kg bw/d) Average exposure, dust: 0.19-0.78 Average exposure, air: 0.002-0.16			
EFSA (2012)	Expert evaluation	Based on analytical data across EU and based on food consumption pattern exposure estimates for PFOA, PFOS and other PFAS were made.	Food (oral) PFOS exposure more than 90% from fish PFOA exposure about 50% from fish + fruit	**PFOS exposure (ng/kg bw/d)** **Mean value** **95-perct value** Infants (range) 0.29-11 (range) 0.7-12 (range) Toddlers 1.2-8.5 (mean) 4.6-13 (mean) Adults 0.8-3.0 (mean) 3.1-6.8 (mean) **PFOA exposure (ng/kg bw/d)** **Mean value** **95-perct value** Infants (range) 0.16-11 (range) 0.46 -15 (range) Toddlers 0.28-10 (mean) 0.58-14 (mean) Adults 0.13-3.2 (mean) 0.28-5.4(mean) **PFHxS exposure (ng/kg bw/d)** **Mean value** **max -**	Infants toddlers adults	+++	

				value Adults Average consumers 0.05-1.22 0.08-1.93 High consumers 0.13-2.25 0.18-3.63			
Selected biomonitoring studies							
Bjerregaard-Olesen et al (2016)	Research paper	Human biomonitoring of PFASs in Aarhus birth-cohort from 2008-2011	-	No exposure calculations, but trends for the exposures in 2009-11	Pregnant women, Aarhus birth cohort (n=1533)	+	Denmark. No exposure calculations
Jensen et al (2015)	Research paper	Human biomonitoring of PFASs in Odense birth-cohort		No exposure calculations	Pregnant women, Odense cohort (n=392)	+	Association was found for miscarriage and exposure to PFNA and PFDA

Mørck et al (2015)	Research paper	Human biomonitoring		No exposure calculations but plasma measurements	Children 6-11 years and their mothers (n=259)	+	Denmark No exposure calculations. Parity a determinant for PFAS
Mogensen et al (2015)	Research paper	Human biomonitoring with focus on exposure from breast milk	Estimation of exposure through breast feeding (30% increase in PFAS per month)	No exposure calculations but serum levels	Birth cohort on Faroe Island (n= 656 children and their mothers)	+	Faroe Island No exposure calculations. Estimation of exposure though brest feeding
Brantsæter et al (2013)	Research paper	Human biomonitoring	Estimations of effect of diet on PFAS levels	No exposure calculations but plasma measurements	Pregnants women Norweigan MoBa chohort (n=487)	+	Norway No exposure calculations. Parity and breast feeding determinants for PFAS levels
Vorkamp et al (2009)	Research paper	Human biomonitoring (PBDEs and PFASs)	-	No exposure calculations but serum measurements	Pregnant women (n=199)	+	Denmark No exposure calculations
Völkel et al (2007)	Research paper	Human biomonitoring in breast milk (pilot study)	Breast milk (oral)	Estimated daily intake for breastfed infant (5 kg): Median: PFOS: 0.10 µg /day	70 Breastmilk samples Germany	++	Germany PFOS and PFOA in breastmilk

				Maximum: PFOA: 0.10 µg /day			
Overall evaluation: Data from DTU Food (2015), Livsmedelsverket (2013), EFSA (2012) and ECHA/RAC (2015) are sufficient for estimating exposure from diet and total exposure. For exposure from indoor environment, another important source, data from NCM (2013) and Danish EPA (2013) may be used. Data indicate that anti-stick cookware, clothes and carpets are not significant sources for PFOA; PFOS and PFHxS exposure. Contribution from drinking water may be relevant. Further food packing materials and carpet sprays are suggested as being potential significant sources.							

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Phthalates – all							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
ECHA 2016	Expert evaluation	Background document for a restriction proposal	Products, food, dust, air	Exposure estimates from articles are based on several recent Danish EPA surveys. Exposure estimates based on modelled data and biomonitoring data are given for DEHP, DBP, DIBP and BBP	Adult, children, infants	+++	
MST 2015	Danish EPA report	Survey and chemical analysis in selected products	Products (various exp routes)	Several phthalates examined in toys and products for use by children. DEHP and DIBP measured in e.g. mobile covers, swimming equipment and doll's heads. Low migration is measured, and these products only make minor contribution to the total exposure to these phthalates.		+++	

MST 2012	Danish EPA report	Literature based calculation of exposure from food, products, dust and air	Food, products, cosmetics, dust, air (various exp routes)	Exposure calculations for DEHP, DINP, DBP, DiBP, BBP, DPP, DnHP, DnOP (see reference for exact values)	Adult women	+++	”Pregnant consumers project”. Intake values based on Fromme et al., 2007
MST 2010	Danish EPA report	Survey and chemical analysis in selected products	Pilates ball, bags shower curtains, floating wings, place mats and vinyl table covers.	DEHP and DIBP detected in pilates ball, bags, shower curtains, floating wings, place mats and vinyl table covers.			
MST 2009	Danish EPA report	Survey and chemical analysis in selected products	Products (various exp routes)	Detection of DBP in clogs. Concluded that single products with high phthalate content may contribute to overall risk	2-year olds	+++	Overview of data in several EPA surveys from 2002-2009
MST 2008	Danish EPA report	Survey and chemical analysis in selected products	Products (various exp routes)	Several phthalates are examined in products for use by infants. DEHP is found in material for baby pram and changing mat. Dimethylphthalat (DMP) 131-11-3 Diethylphthalat (DEP) 84-66-2 Diisobutylphthalat (DIBP) 84-69-5 Dibutylphthalat (DBP) 84-74-2 Butylbenzylphthalat (BBP) 85-68-7 Di-(2-ethylhexyl)-phthalat (DEHP) 117-81-7 Di-n-octylphthalat (DNOP) 117-84-0 Di-iso-nonylphthalat (DINP) 28553-12-0 Di-isodecylphthalat (DIDP) 26761-40-0		+	
MST data-	Danish	Surveys and chemical analy-		In the Danish database on consumer product		+/+++	Some reports may

base	EPA reports	sis in selected products		many products containing DEHP are found, and several products may be relevant to children and possibly the unborn child.			include exposure assessment. Some data are included in project on 2-year olds and pregnant consumers
Lee et al 2014	Research paper	Modelling of exposure based on intake and concentration data (food, dust, soil) and comparison with biomonitoring	Food, dust (oral)	Exposure calculations for DEHP, DBP, BBP, (mean, median, 95-percentile) (see paper for exact values)	Children 2 years old	+++	Comparison of Denmark and South Korea
Fromme et al., 2007	Research paper	Measurement of phthalate intake in duplicate diet samples	Food (oral)	Diet (average and high): DMP, DEP, DAP, DnBP, DiBP, DnPP, DCHP, BBP, DEHP, DPheP, DPHP. (see paper for exact values)	Adult	+++	Germany (2005)
Fromme 2013	Research paper	Exposure calculation based on duplicate diet and comparison with biomonitoring	Food (oral)	Diet (average and high): DMP, DEP, DAP, DPropP, DnBP, DiBP, DnPP, DCHP, BBP, DEHP, DnOP, DPheP, DiNP, DiDP, DnDP, DPHP (see paper for exact values). Biomonitoring (“average” and “high”) (DEP, DnBP, DiBP, BBP, DEHP, DINP). Comparison with other estimates of dietary exposure (Table 4)	Children 15-21 month of age	+++	Germany (2009-2010)
Sakhi 2014	Research paper	Calculation of intake based on concentration data on phthalates in food	Food (oral)	Exposure calculations for DMP, DEP, DiBP, DnBP, BBzP, DEHP, DCHP, DnOP, DiNP, DiDP (mean, median, 95-percentile) (see paper for exact values). Comparison with other estimates of dietary exposure (Table 6)	Adult	+++	Norway (2010-2011)

Sioen 2012	Research paper	Exposure calculations based on concentrations in food and food consumption of preschool children and adults	Food (oral)	Exposure calculations for DMP, DEP, DiBP, DnBP, BBzP, DEHP, DCHP, DnOP, (median, 95-percentile) (see paper for exact values).	Adult, children 2.5-6 years	+++	Belgium (2004)
Bradley 2013	Research paper	Concentration data on phthalates in food	Food (oral)	Calculated exposure for different age groups (DEP, DiBP, DBP, BBP, DEHP). Toddlers: Age > 1.5 to 2.5 years DEP 0.3‑0.8, DIBP 1.4‑2.7, DBP 0.4‑1.0, BBP 0.07‑1.3, DEHP 6.9‑9.9 ug/kg bw/day. See paper for other values.	Adult, children e.g. 1.5 to 2.5 years	++	UK
Langer 2010	Research paper	Measurement of dust in children's homes and day-care facilities	Dust (oral, inh)	No calculation of exposure		+	Lack of calculated exposure
Bekö 2013	Research paper	Modelling of exposure based on intake and concentration data (food, dust, soil) and comparison with biomonitor-ing	Dust, air, (0ral, dermal,inh)	Exposure calculation for DEHP, DnBP, DiBP, BBP, DEHP (mean, median, 95-percentile) (see paper for exact values) Comparison with other biomonitoring data (Table 9)	Children 3-6 years	+++	Denmark
BfR 2011	Report from Ger-man Fed-eral Insti-tute for Risk As-sessment (BfR)	Measurement of DPHP in toys	Toys (oral, der-mal)	10-48% content of DPHP in four specific toys for children under 3 years of age (shower gel con-tainer formed as toy; baby toilet seat, bath-duck, tyre of toycar). Calculation of exposure of child 7.5 kg bw. Exposure up to 135 ug/kg bw/day.	Children below 3 years	+++	German language report with English abstract. DPHP possibly also found in toys by CPSC and CVUS Stuttgart. ECHA: DPHP is explicitly not promoted by its manufacturers

							for use in toys, food packaging or medical products.
Selected biomonitoring data							
Callesen 2014	Research study	Biomonitoring, Denmark		No calculation of exposure, but urinary concentrations	Children 3-5 years	+	Lack of calculated exposure
Frederiksen 2014	Research study	Biomonitoring, Denmark		No calculation of exposure, but urinary concentrations (DEP, DnBP, DiBP, BBP, DPP, DEHP, DOP, DiNP, DiDP)	Pregnant women, children	+	Lack of calculated exposure
Langer 2014	Research study	Biomonitoring, Denmark		No calculation of exposure, but urinary concentrations. Comparison with other biomonitoring data for children (table 4) and dust levels from Langer et al 2010	Children 3-6 years	+	Lack of calculated exposure
Larsson 2014	Research study	Biomonitoring, Sweden, Parabens, phthalates, bpa, triclosan		No calculation of exposure, but urinary concentrations	Adult women, children 6-11 years	+	Lack of calculated exposure
Frederiksen 2013	Research study	Biomonitoring, Denmark		Exposure calculations for DiBP, DBP, BBzP, DEHP, DINP, BPA (see reference for exact values)	Adult women, children 6-11 years	+++	Denmark
Frederiksen 2011	Research study	Biomonitoring, Denmark		No calculation of exposure, but urinary concentrations (DEP, DnBP, DiBP, BBP, DPP, DEHP, DOP, DiNP, DiDP)	Pregnant women, children	+	Lack of calculated exposure
Boas 2010	Research study	Biomonitoring, Denmark		No calculation of exposure, but urinary concentrations (DEP, DBP, DBzP, DEHP, DnOP, DiNP)	Children 4-9 years	+	Lack of calculated exposure

Schlumpf 2010	Research study	Biomonitoring		Exposure estimates for intake by infants	Infants/milk	++	CH 2004-2006
Overall evaluation: The data from several publications contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. In the Danish database on consumer product many products mainly containing DEHP are found, and only sparse data for the other phthalates could be found.							

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Siloxane D4							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
ECHA 2016	Expert evaluation	RAC/SEAC opinion on D4 and D5	(various exp routes)	It is evaluated that main exposure route of consumers is via personal care products. No data for consumer exposure to D4 are listed, as personal care products are not within REACH regulations.		+	Lack of exposure data
Biesterbos 2015	Research paper	Human volunteer study on dermal exposure to cyclic siloxanes	(dermal, inhalation)	No data available		+	Indications that inhalation exposure may contribute more to internal dose than dermal exposure
Tran 2015	Research paper	Measurement of siloxanes in indoor dust		Human exposure calculations only for total siloxanes. Not specific data to calculate human exposure to D4.	Adult, children	+ Indoor dust	12 countries. Lack of data for calculation of D4 exposure
MST 2014	Danish EPA report	Review of other reports		No data available		+	Concludes that no adequate exposure data could be obtained. Refers

							measured D4 in human breastmilk
Pieri 2013	Research paper	Exposure calculation based on measurements in indoor air	Air (inh)	Indoor air: Exposure calculations for children and adults (in ug/day for total siloxanes, needs recalculation, see paper for exact figures). E.g. 1500 ug/day for adults = 25 ug/kg bw/day for a 60 kg woman of which approximately 20% D4 (5 ug/kg bw/day)	Adult, children	++ Indoor air	UK and Italy. Needs further calculations
MST 2012	Danish EPA report	Literature based calculation of exposure from cosmetics. Measured data for concentrations of D4 in specific products for this report.	Cosmetics (dermal), air (inh)	Basic scenario (body lotions) Mean: 0.003 ug/kg bw/day High: 0.005 ug/kg bw/day Scenario using sunscreen Mean: 10.2 ug/kg bw/day High: 20.4 ug/kg bw/day No data for indoor air	Adult women	+++ Total; cosmetics	”Pregnant consumers project”. High exposures are based on twice as frequent use as mean exposure. Much lower values than SCCS due to low measured concentrations in products
SCCS 2010	Expert evaluation	Exposure calculation based on use of cosmetic products containing average concentration of D4 and D5	Cosmetics (dermal)	Cosmetic products other than sunscreens: Systemic exposure dose 100 ug/kg bw/day Including sunscreens: Systemic exposure dose 200 ug/kg bw/day	Adult	+++	Conservative values for total D5 and D4 and overestimation of dermal uptake
Selected biomonitoring studies							

Hanssen 2013	Research paper	Biomonitoring in pregnant and postmenopausal women		No data for calculation of exposure, but blood measurements	Women	+ Total	Norway. Lack of calculated exposure
Overall evaluation: The data from MST 2012 and SCCS 2010 contain sufficient data for making exposure estimates for this project. Systemic exposure values differed in these two reports and further decisions on exposure calculations are needed. Literature search revealed information that air may contribute to human exposure. Data for children are lacking							

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Triclosan							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST 2012	Danish EPA report	Literature based calculation of exposure from cosmetics. Conservative approach combining mean/maximal exposure values and maximum permitted levels	Dust, cosmetics (oral)	Dust (ug/kg bw/day): Mean: 0.0015, high 0.0002 Cosmetics (toothpaste and deodorant, ug/kg bw/day): mean 13, high 23	Pregnant women	+++	”Pregnant consumers project”. Conservative values
SCCP 2009	Expert evaluation	Conservative approach combining maximal exposure values and maximum permitted levels	Cosmetics (oral, dermal)	High: 300 or 526 ug/kg bw/day	Adult	+++	Conservative values. Addendum 2011
MST 2007	Danish EPA report	Survey of use of triclosan and chemical analysis of selected products		Triclosan detected in deodorants		+	
MST 2006	Danish EPA report	Survey of use of triclosan and chemical analysis of selected products		Triclosan detected in antibacterial soap		+	
MST 2002a	Danish EPA report	Survey of use of triclosan and chemical analysis of selected products		Triclosan detected in sportssocks		+	
MST 2003	Danish EPA report	Survey of use of triclosan and chemical analysis of		Triclosan detected in clothes (low concentrations). Sandals, underwear, sportswear (bicycle		+	

		selected products		shorts). Reported use of triclosan for textile for hospital workers, sports clothes, bedlinen etc.			
MST 2002b	Danish EPA report	Survey of use of triclosan and chemical analysis of selected products		Triclosan not detected in carpets		+	
Selected biomonitoring studies							
Lassen et al 2016	Research paper	Biomonitoring, Denmark		No exposure estimates	Pregnant women	+	Lack of calculated human exposure
Geens et al 2015	Research paper	Biomonitoring in Belgian sub-population (obese), 24h urine samples.		Daily intake (ug/kg bw/day) calculated to be, mean: 0,49, median: 0.017, high: 0.565	Adults, obese sub-population, but no differences in exposure compared to the lean control group.	++	Biomonitoring data (in both ng/mL and ug/g creatinine) to calculate expected exposure. Their TCS exposure medians are 1.5 ng/mL and 1.4 ug/g creatinine
Frederiksen 2014	Research paper	Overview of biomonitoring data 2006-2012		No exposure estimates	Children, women	+	Lack of exposure calculations
Frederiksen et al 2013a	Research paper	Biomonitoring, Denmark		No exposure estimates	Adult women, children 6-11 years	+	
Frederiksen et al 2013b	Research paper	Biomonitoring, Denmark		No exposure estimates	Children and Ado-lescents	+	Lack of calculated human exposure

Pirard 2012	Research paper	Biomonitoring		No exposure estimates	Adult, children	+	Belgium. Lack of calculated exposure
Casas et al 2011	Research paper	Biomonitoring, Spain		Nno exposure estimates	Pregnant women and 4-year old children	+	Lack of calculated human exposure
Overall evaluation: The data from MST 2012 and SCCP 2009 contain data considered sufficient for making exposure estimates for this project. In the Danish database on consumer products it is noted that triclosan was examined in several projects, and was found in deodorants and clothes.							

References:
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Casas L, Fernández MF, Llop S, Guxens M, Ballester F, Olea N, Irurzun MB, Rodríguez LS, Riaño I, Tardón A, Vrijheid M, Calafat AM, Sunyer J; INMA Project. Urinary concentrations of phthalates and phenols in a population of Spanish pregnant women and children. Environ Int. 2011 Jul;37(5):858-66.

UV filter – OMC							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/ high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST (2015)	Danish EPA report	Literature based calculation of exposure from cosmetics. Conservative approach combining mean/maximal exposure values and maximum permitted levels.	Cosmetics (dermal)	The identification of exposure levels has to be examined further, see comments	Adult	+++	10% in sunscreen; 10% in other products. Higher than MST 2012 due to higher amounts of product and higher dermal absorption.
MST (2012)	Danish EPA report	Literature based calculation of exposure from cosmetics. Conservative approach combining mean/maximal exposure values and maximum permitted levels (or half the permitted levels)	Cosmetics (dermal)	The identification of exposure levels has to be examined further, see comments	Adult women	+++	”Pregnant consumers project”. Mean and high exposures are based on the same use scenario but different OMC concentrations in products. No notes of OMC use in other product types

Selected biomonitoring studies							
Manova (2015)	Research study	Modelling of human exposure based on use of products		Exposure estimates are available for several age groups (see paper for exact figures)	Children, several age groups, women	++	Swiss data
Krause (2012)	Research study	Biomonitoring		No exposure estimates. Table comparing concentrations in different biomonitoring studies	Adult women	+	DK 2004-2008
Schlumpf (2010)	Research study	Biomonitoring		Exposure estimates for intake by infants	Infants/milk	++	CH 2004-2006
Overall evaluation: The data from MST 2012 and MST 2015 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. Due to a recent elaborate MST report including OMC exposure evaluation, literature search is limited to recent Danish biomonitoring data and to child-specific European data. References for biomonitoring data included in MST report are listed.							

References:

Krause M, Klit A, Blomberg Jensen M, Søeborg T, Frederiksen H, Schlumpf M, Lichtensteiger W, Skakkebaek NE, Drzewiecki KT. Sunscreens: are they beneficial for health? An overview of endocrine disrupting properties of UV-filters. Int J Androl. 2012 Jun;35(3):424-36.

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UV filter – BP-3							
Reference	**Type of study**	**Method/content**	**Exposure sources** (exposure routes)	**Exposure contribution from specific sources/total exposure** (mean-typical/high)	**Target groups**	**Relevance for exposure assessment in this project**	**Comments**
MST (2015)	Danish EPA report	Literature based calculation of exposure from cosmetics. Conservative approach combining mean/maximal exposure values and maximum permitted levels	Cosmetics (dermal)	Scenario using sunscreen (18 g per day): 3 mg/kg bw/day for adult Scenario for "other products" (lower concentrations allowed): 0.12 mg/kg bw/day for adult	Adult	+++	10% in sunscreen according to this report, but recently maximum permitted level is changed to 6%; 0.5% in other products
MST (2012)	Danish EPA report	Literature based calculation of exposure from cosmetics. Conservative approach combining mean/maximal exposure values and maximum permitted levels (or half the permitted levels). Overview table on biomonitoring data	Cosmetics (dermal)	Basic scenario Mean: 48 ug/kg bw/day High: 96 ug/kg bw/day Scenario using sunscreen Mean: 600 ug/kg bw/day High: 2400 ug/kg bw/day Biomonitoring data are listed as urinary content	Adult women	+++	"Pregnant consumers project". Mean and high exposures are based on the same use scenario but different BP-3 concentrations in products. Noted that BP-3 may be used in paints, plastic,

							food packaging
Selected biomonitoring studies							
Guidry (2015)	Research study	Biomonitoring		ND, no exposure estimates	Children, mothers	-	Lack of exposure calculations. Norway
Dewalque (2014)	Research study	Biomonitoring		ND, no exposure estimates	Children, women	-	Lack of exposure calculations. BE data 2013
CDC (2014)				May contain exposure data	Children >6 y	-	US data 2005-10
Demo-cophes 2013				Exposure calculation performed	Children >6y, Mothers	++/+++	DK 2010-2012
Frederiksen (2014)		Overview of biomonitoring data 2006-2012		ND, no exposure estimates	Children, women	-	Lack of exposure calculations
Frederiksen (2013)	Research study	Biomonitoring		ND, no exposure estimates	Children, mothers	+	Lack of exposure calculations for BP-3
Krause (2012)	Research study	Biomonitoring		No exposure estimates. Table comparing concentrations in different biomonitoring studies	Adult women	+	DK, US, FR data 2003-6
Schlumpf (2010)	Research study	Biomonitoring		Lack of calculated exposure	Infants/breast milk	++	CH data 2004-2006
Overall evaluation: The data from MST 2012 and MST 2015 contain updated data of high quality and the data are considered sufficient for making exposure estimates for this project. Due to a recent elaborated MST report including BP-3 exposure evaluation, literature search is limited to recent Danish biomonitoring data and to child-specific European data. References for biomonitoring data included in MST report are listed.							

References:

CDC 2014 referenced by MST 2015 as: CDC (2014). Fourth National Report on Human Exposure to Environmental Chemicals. Updated Tables, August, 2014. U.S. Department of Health and Human Services. Centers for Disease Control and Prevention.

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Manová E, von Goetz N, Hungerbuehler K. Aggregate consumer exposure to UV filter ethylhexyl methoxycinnamate via personal care products. Environ Int. 2015 Jan;74:249-57.

MST 2012: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer

MST 2015: Kortlægning af kemiske stoffer I forbrugerprodukter nr. 142, 2015. Kortlægning og sundhedsmæssig vurdering af UV-filtre

Schlumpf M, Kypke K, Wittassek M, Angerer J, Mascher H, Mascher D, Vökt C, Birchler M, Lichtensteiger W. Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere. 2010 Nov;81(10):1171-83.

Appendix 5

Regulatory overview of the selected substances

Objective

As part of the project an overview of regulation of the selected substances will be given. The table below gives a summary overview of the regulatory status of each of selected substances in chapter 2 and for which expsoure data was found in chapter 3. The regulatory overview covers the various sectors of regulation (industrial chemicals, food and food contact materials, cosmetics, biocides/pesticides, limit values in drinking water, soil and air):

- The EU-harmonised classification according to the CLP regulation Annex VI. Relevant classifications in relation to systemic effects are indicated (i.e. CMR effects, Acute tox, STOT SE, STOT RE), as only these classifications may cover either effects in relation to endocrine disruption and/or neurotoxic effects.
- Regulations in relation to food items i.e. as additive or as contaminant, or in relation to food contact materials e.g. migration limits.
- Regulation for cosmetics i.e. whether the substances are subject to provisions in annex II-VIVI of the cosmetic regulation EC No 1223/ 2009.
- Regulation of toys regarding maximum contents or migrations limits
- If the substance is covered by the biocide og pesticides regulation
- If the substance is subject to restrictions under REACH (Annex XVII) or identified as an SVHC substance and included on the Candidate List or on the AuthorisationAuthorisation List of REACH (Annex XIV).).
- If the substance is regulated by human health based quality criteria / limit values in drinking water, soil or air (national values or EU-values).

Having an overview for a substance in these regulatory areas will give some information regarding the severity of the human health effects and also give an indication of the potential sources of exposure and to which extent the consumer is be protected against the exposure.

Table 5.1 Overview of the regulation for the selected substances

Substance/CAS	CLP – Classification with regard to: CMR Acute tox STOT SE STOT RE	REACH (restrictions, including the list of candidate substances or the authorization list)	Food[i]	Cosmetics[ii]	Toys[iii]	Biocides[iv], Pesticides	Limit value in soil[v] / air (B-value)/drinking water (at the tap)	Comments
Antioxidants								
Butylated hydroxyanisole (BHA)/ 25013-16-5	-	-	Specific migration limit in plastic-FCM: 30 mg/kg food. Must not be technologically functional in the food. Permitted as a food additive in chewing gum and in industrially applied deep fat frying.	-	-	Not a biocide or a pesticide	Phenols: 70 mg/kg dry matter in soil 0.5 µg/l drinking water.	

Butylated hydroxytoluene (BHT) = 2,6-Di-tert-butyl-p-cresol (DBPC)/ 128-37-0	-	-	Specific migration limit in plastic-FCM: 3 mg/kg food. Must not be technologically functional in the food. Permitted as a food additive in chewing gum and in industrially applied deep fat frying.	-	-	Not a biocide or a pesticide	Phenols: 70 mg/kg dry matter soil, 0.5 µg/l drinking water, 0.01 mg/m^3 air	
Brominated substances								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
TBBPA (Tetrabromobisphenol A)/ 79-94-7	-	-	-	-	-	Not a biocide or a pesticide.	-	
HBCDD/ 3194-55-6/ 25637-99-4/ 134237-50-6/ 134237-51-7/ 134237-52-8	Rep 2 Lact.	On the authorization and the candidate list.	-	CMR-reg	CMR-reg	Not a biocide or a pesticide.	-	
Deca-BDE/ 1163-19-5	-	On the candidate list.	-	-	-	Not a biocide or a pesticide	-	
BDE-47 og BDE-99/ 32534-81-9	Lact STOT RE 2	-	-	-	-	Not a biocide or a pesticide	-	

Chlorinated substances								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
Dioxiner og dioxinlignende PCB'er	PCB: R33 (kumulerer)	-	Limit values in a host of foods are found.[vi]	On the prohibition list, annex II	-	Not a biocide or a pesticide.	Quality criteria in soil not relevant in connection with soil ingestion. -	
Tetrachloroethylene/ 127-18-4	Carc 2	-	-	On the prohibition list, annex II	CMR-reg	Not a biocide or a pesticide.	5 mg/kg dry matter soil 1 µg/l drinking water 0.006 mg/m^3 evaporation criterion, 0.01 mg/m^3 (C-value).	
tris(2-chloroethyl) phosphate (TCEP)/ 115-96-8	Carc 2, Repr. 1B, Acute tox 4.	On the candidate and authorization list	-	On the prohibition list, annex II	No more than 5 ppm in toys for children under 3, and for toys intended to be mouthed.	Not a biocide or a pesticide.	-	
Fluorinated substances								
Perfluorooctanoate,PFOA/ 335-67-1	Carc2 Rep. 1B, Lact. STOT RE 1	On the candidate list.	Ammonium per-fluorooctanoate must only be applied on reused items which are sintered at hight tempepratures.	CMR-reg	CMR-reg	Not a biocide or a pesticide.	Sum of 12 perfluorinated alkyl acid substances: PFBS, PFHxS, PFOS, PFOSA, 6:2 FTS, PFBA, PFPeA, PFHxA, PFHpA, PFOA, PFNA, PFDA: 0.4 mg/kg dry matter soil, 0.1 µg/l drinking water	
Perfluorooctansulfonat, PFOS/ 2795-39-3	Carc2 Rep. 1B, Lact. STOT RE 1	-	-	CMR-reg	CMR-reg	Not a biocide or a pesticide		
PFHxS/ 355-46-4	-	-		-	-	Not a biocide or a pesticide		

Hydrocarbons								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
n-hexane / 110-54-3	Repr.2 STOT RE 2 STOT SE 3	-	Højst 5 mg/kg i fedtfri cerealiekim, 1 mg/kg i fedtstof, olie eller kakaosmør, 10 mg/kg i fødevaren, der indeholder det fedtfri proteinprodukt og det fedtfri mel, 30 mg/kg i det fedtfri sojaprodukt, der sælges til den endelige forbruger. Maks. 1 mg/kg fødevare fra aromastof.	On the prohibition list, annex II	CMR-reg	Not a biocide or a pesticide.	*Sum of hydrocarbons:* *Soil:* Volatile hydrocarbons, C_6-C_{10}: 25 mg/kg dry matter soil. *Air:* Evaporation criterion and C-value for sum of C7-C12 hydrocarbons incl. aromate fraction : 0.2 mg/m^3. Evaporation criterion for sum of C_6-C_{35} kulbrinter: 0.1 mg/m^3 Evaporation criterion for C9-C10 alkyl benzenes: 0.03 mg/m^3 C9 aromates: 0.03 mg/m^3 (C-values) n-hexane 0.4 mg/m^3 (C-value) n-heptane 1 mg/m^3 (C-value) Toluene 0.4 mg/m^3 (C-value and evaporation criterion) 25 mg/L Drinking water criterion Xylenes 0.1 mg/m^3 (C-value and evaporation criterion) Ethyl benzene 0.2 mg/m^3 (C-value) Styrene 0.2 mg/m^3 (C-	
n-heptan/ 142-82-5	-	-	-	-	-	Not a biocide or a pesticide		
Toluen/ 108-88-3	Repr. 2, STOT RE 2, STOT SE 3	More than 0.1% prohibited in adhesive and spray paint for private households.	-	Prohibited, with the exception of up to 25% in nail product for adults.	CMR-reg	Not a biocide or a pesticide		
Xylenes/ 1330-20-7	Acute tox. 4	-	-	-	-	Not a biocide or a pesticide.		
Ethylbenzene/ 100-41-4	Acute tox. 4,	-	-	-	-	Not a biocide or a pesticide.		

Styren/ 100-42-5	Acute tox. 4, STOT RE 1, Repr. 2		Permitted as monomeric substance to used in FCM	CMR-reg	CMR-reg	Not a biocide or a pesticide.	value and evaporation criterion) White spirit, aromate containing: 0.2 mg/m^3 (C-value and evaporation criterion *Drinking water:* C9-alkyl benzenes: 1 µg/l Styrene: 1 µg/l Toluene: 25 mg/L	
Methylstyrene/ 1319-73-9	-	-	-	-	-	Not a biocide or a pesticide.		
Propyl benzene/ 103-65-1	STOT SE 3	-	-	-	-	Not a biocide or a pesticide.		
1,2,4-Trimethylbenzen/ 95-63-6	Acute Tox 4 STOT SE 3	-	-	-	-	Not a biocide or a pesticide		
Diisopropylbenzen/ 25321-09-9	-	-	-	-	-	Not a biocide or a pesticide.		
Phenyloctan/2189-60-8	-	-	-	-	-	Not a biocide or a pesticide		
White spirit C7-C12 hydrocarbons/ 64742-82-1	STOT RE 1	-	-	-		Not a biocide or a pesticide.		
Metals								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
Lead and lead compounds	Repr. 1A; H360D STOT RE 2	Certain lead compounds are on the candidate and authorization list. Lead carbonates and sulphates are prohibited in paint. Prohibited in jewellery and	Limit values for a host of foods exist.[vii]	On the prohibition list, annex II.	Migration limits apply dependent on type of toy.	Not a biocide or a pesticide.	Inorganic lead 40 mg/kg dry matter in soil, 10 µg/l drinking water. 0.0004 mg/m^3 (C-value, inorganic dust) 0.0005 mg/m^3 (year value outdoor air)	All limit values measured as Pb.

		articles, or touchable parts, which may be mouthed by children: > 0,05%. Prohibition against lead content of other articles are currently under negotiation.						
Mercury and compounds	STOT RE 1, Repr. 1B, Acute tox 2.	Prohibited in thermometers and other meters.	Limit values for a host of foods exist.[viii]	Prohibited, except up to 0.007 % (as Hg) in eye products.	Migration limits apply dependent on type of toy.	Not a biocide or a pesticide.	Inorganic mercury: 1 mg/kg dry matter soil, 1 µg/kg drinking water 0.0001 mg/m^3 (C-value, inorganic dust)	
Aluminium and compounds	-	-	Permitted as food additive.	Permitted, in some instances with limitations.	Migration limits apply dependent on type of toy.	Aluminium phosphide approved as product type 14, 18 and 20. A couple of other aluminium compounds are in the application phase. There are products on the DK market both as pesticide and biocide.	200 µg/l drinking water 0.01 mg/m^3 (C-value)	
Medicines								
Paracetamol/ 103-90-2	-	-	-	-	-	Not a biocide or a pesticide.	-	
Parabens								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
Propylparaben (PP)/ 94-13-3	-	-	Permitted in FCM	DK: Prohibited for children under 3 years.[ix] EU: Not to be used in leave-on	-	Not a biocide or a pesticide.	-	

				products designed for application on the nappy area of children under three years of age. EU max conc. 0.14% for PP+BP.				
Butylparaben (BP)/ 94-26-8	-	-	-	DK: Prohibited for children under 3 years.[x] EU: Not to be used in leave-on products designed for application on the nappy area of children under three years of age EU max conc. 0.14% for PP+BP	-	Not a biocide or a pesticide.	-	
Isobutylparaben/ 4247-02-3	-	-	-	Prohibited in EU.	-	Not a biocide or a pesticide.	-	
Pesticider								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
Pirimiphos-methyl/29232-93-7	Acute Tox. 4	-	-	-	-	Not a biocide. No approvals as pesticide in DK. Approved as pesticide in other EU member states.	*In general:* Pesticides, sum: 0.5 µg/l drinking water, Single pesticide: 0.1 µg/l drinking water. There is no soil quality criterion in general for all pesticides. The measured concentration of pesticide in soil must	Maximum residues limits for various crops and produce are not included in this table, but can be looked up in the Maximum residue levels of pesticides database: http://ec.europa.eu/f
Procymidon/ 32809-16-8	-	-	-	-	-	Not a biocide. No approvals as pesticide in DK. Not approved as pesticide in EU		

						since 2008.	undergo a concrete evaluation.	ood/plant/pesticides/eu-pesticides-database-redirect/index_en.htm
Mancozeb/ 8018-01-7	Repr. 2	-		CMR-reg.	CMR-reg	Not a biocide. Approved as pesticide (fungicide) in DK. Approved as pesticide in other EU member states.		
Maneb/ 12427-38-2,	Acute Tox. 4, Repr. 2		-	CMR-reg.	CMR-reg	Not a biocide. Approved as pesticide (fungicide) in DK. Approved as pesticide in other EU member states.		
Propineb/ 12071-83-9	-		-	-	-	Not a biocide. Not approved as pesticide in DK since 1999. Approved as pesticide in other EU member states.		
Diazinon/ 333-41-5	Acute Tox. 4					Not approved as biocide in DK since 2002. Not approved as pesticide in DK since 2002. Not approved as pesticide in EU since 2007.		
Dimethoat/60-51-5	Acute Tox 4					Not approved as biocide in DK since 1998. Not approved as pesticide since 2013 in DK. Approved as pesticide in other EU member		

						states.		
Carbaryl/63-25-2	Acute Tox. 4 Carc 2					Not approved as biocide in DK since 1990. Not approved as pesticide in DK since 1993. Not approved as pesticide in EU since 2007.		
Chlorfenvinfos/470-90-6	Acute Tox 2 and 3					Not a biocide. No approvals as pesticide in DK. Not approved as pesticide in EU since 2007.		
Benomyl/17804-35-2	STOT SE 3 Muta 1B Repr. 1B			CMR-reg.	CMR-reg	Not a biocide. No approvals as pesticide in DK. Not approved as pesticide in EU since 2003.		
Linuron/330-55-2	Acute Tox. 4 Carc 2 Repr. 1B STOT RE 2			CMR-reg.	CMR-reg	Not a biocide. Not approved as pesticide in DK since 2001. Approved as pesticide in other EU member states.		
Methomyl/16752-77-5	Acute Tox 2					Not approved as biocide in DK since 2000. Not approved as pesticide in DK since 1996. Approved as pesticide in other EU member states.		
Methamidophos/ 10265-92-6	Acute Tox 2 og 3					Not a biocide. No approvals as pesticide in DK. Not approved as a pesticide in EU since 2008.		

Oxydemeton-methyl/ 301-12-2	Acute Tox 3					Not a biocide. Not approved as pesticide in DK since 1995. Not approved as a pesticide in EU since 2007..		
Phenolic compounds								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
Bisphenol A/ 80-05-7	Rep 2	-	Specific migration limit in plastic-FCM: 0,6 mg/kg. Expected to be reduced to 0.05 mg/kg food. Must not be used for polycarbonate bottles for babies.	On the prohibition list, annex II	0.1 mg/l (migration value)	Not a biocide or a pesticide	Administratively covered under "Other phenols": 0.5 µg/l drinking water	Current CLH proposal: Rep 1B
Bisphenol F/ 87139-40-0	-	-	-	-	-	Not a biocide or a pesticide.	*As Bisphenol A*	
Bisphenol S/ 80-09-1	-	-	Specific migration limit in plastic-FM: 0.05 mg/kg food.	-	-	Not a biocide or a pesticide.	*As Bisphenol A*	
Nonylphenol/ 25154-52-3	Rep 2	Must not be used in a host of products in concentrations of more than 0,1%.	-	On the prohibition list, annex II	CMR-reg	Not a biocide or a pesticide.	25 mg/kg dry matter in soil, 20 µg/l drinking water 0.02 mg/m^3 in air (C-value) and as evaporation criterion.	
Phthalates								
DEHP (di-ethyl-hexyl-phthalate)/ 117-81-7	Rep. 1B	Max. 0.1% of softened material in toys and articles for small children. On the candidate and the authorization lists.	1.5 mg/kg food from plastic-FCM[xi]	On the prohibition list, annex II	Max. 0.1% in toys and child care articles	Not a biocide or a pesticide.	25 mg/kg dry matter in soil. 0.005 mg/m^3 air. 1 µg/l drinking water	The REACH restriction is the source of the toys restriction.

Substance/CAS	CLP- classifi-cation	REACH	Food	Cosmetics	Toys	Biocides, Pesticides	Limit values	Comments
DINP (di-iso-nonyl-phthalate)/ 28553-12-0 og 68515-48-0	-	Max. 0.1% of softened material in toys and articles for small children.	9 mg/kg food from plastic-FCM[1] (together with DIDP)	-	Max. 0.1% in toys and child care articles.	Not a biocide or a pesticide	<u>Sum of other phthalates</u> (except DEHP): In soil: 250 mg/kg dry matter 0.01 mg/m^3 air 5 µg/l drinking water	The REACH restriction is the source of the toys restriction.
DBP (di-butyl-phthalat)/ 84-74-2	Rep. 1B	Max. 0.1% of softened material in toys and articles for small children. On the candidate and the authorization lists.	0.3 mg/kg food from plastic-FCM[1]	On the prohibition list, annex II	Max. 0.1% in toys and child care articles.	Not a biocide or a pesticide		The REACH restriction is the source of the toys restriction.
DIBP (di-iso-butyl-phthalat) / 84-69-5	Rep. 1B	On the candidate and the authorization lists.	Not permitted.	CMR-reg.	Max. 0,05%[xii] in toys and childcare articles for children under 3 years.	Not a biocide or a pesticide		
BBP (butyl-benzyl-phthalat)/ 85-68-7	Rep. 1B	Max. 0.1% of softened material in toys and articles for small children. On the candidate and the authorization lists.	30 mg/kg food from plastic-FCM[1]	On the prohibition list, annex II	Max. 0.1 in toys and child care articles .	Not a biocide or a pesticide.		The REACH restriction is the source of the toys restriction.
DPP (Dipentyl phthalate) / 131-18-0	Rep. 1B	On the candidate list.	Not permitted.	On the prohibition list, annex II	Max. 0.05% [XII] in toys and childcare articles for children under 3 years.	Not a biocide or a pesticide.		
Di-n-hexyl phthalate / 84-75-3	Rep 1B	-	Not permitted.	CMR-reg.	Max. 0.05%[XII] in toys and childcare articles for children under 3 years.	Not a biocide or a pesticide.		
Di-n-octyl phthalate (DnOP)/ 117-84-0	-	Max. 0.1% of softened material in toys and articles for small children.	Not permitted.	-	Max. 0.1% in toys and child care articles	Not a biocide or a pesticide.		The REACH restriction is the source of the toys restriction.
Di-cyclo-hexyl-phthalat (DCHP)/ 84-61-7	-	-	Not permitted.	-	Max. 0.05%[XII] in toys and childcare articles for children under 3 years.	Not a biocide or a pesticide.		

di-2-propylheptyl phthalate (DPHP)/ 53306-54-0	-	-	Not permitted.	-	Max. 0.05%[XII] in toys and childcare articles for children under 3 years.	Not a biocide or a pesticide.		
UV-filters								
Substance/CAS	**CLP- classifi-cation**	**REACH**	**Food**	**Cosmetics**	**Toys**	**Biocides, Pesticides**	**Limit values**	**Comments**
OMC, octyl methoxycinnamat, 2-ethylhexyl-4-methoxycinnamat/ 5466-77-3	-	-	-	10%	-	Not a biocide or a pesticide	-	
Benzophenone 3 (BP-3)/ 131-57-7	-	-	Permitted in plastic-FCM	Max conc of 0.5% as absorber, otherwhise permitted up to 6%	-	Not a biocide or a pesticide	-	
Other substances								
Acrylamide/ 79-06-1	Muta 1B, Repr. 2, Carc 1B, STOT RE 1, Acute Tox 3	On the candidate list and must not be used in in conc. Larger than 0.15 in injection- and caulking agents.	-	On the prohibition list, annex II	CMR-reg	Not a biocide or a pesticide.	0.1 µg/l drinking water 0.0002 mg/m^3 (C-value)	
Octamethylcyclo-tetrasiloxan, D4/ 556-67-2	Repr. 2	-	-	CMR- reg.	CMR-reg	Not a biocide or a pesticide	0,01 mg/m^3 (C-value)	Current restriction proposal: max 0.1% in wash-off personal care products
Triclosan/ 3380-34-5	-	-	-	Permitted with up to 0.3% in toothpaste, soap, deodorant etc. Up to 0.2% in mouth washes.	-	Not approved or a pesticide	-	

C-value (Contribution-value) in air, in Danish B-værdi (Bidragsværdi)

FCM: Food Contact Material

" - " : not specifically regulated under that particular application.

[i] **Food:** Bekendtgørelse nr 1044 af 04/09/2015 om tilsætninger mv. til fødevarer. Sets limits for e.g. **n-hexane** after use as extraction agent for aromas, fat-free cereal germ, manufacture or fractionation of fats and oils, and manufacture of cocoa butter, and preparation of fat-free protein products and fat-free flour. https://www.retsinformation.dk/Forms/R0710.aspx?id=174202

Fødevarekontaktmaterialer (FKM), generelt: *EUROPA-PARLAMENTETS OG RÅDETS FORORDNING (EF) nr. 1935/2004 af 27. oktober 2004 om materialer og genstande bestemt til kontakt med fødevarer og om ophævelse af direktiv 80/590/EØF og 89/109/EØF.* Giver ingen konkrete grænseværdier, men bestemmer at FKM ikke må "frembyde en fare for menneskers sundhed". http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2004R1935:20090807:DA:PDF

FKM, plastik: *KOMMISSIONENS FORORDNING (EU) Nr. 10/2011 af 14. januar 2011 om plastmaterialer og -genstande bestemt til kontakt med fødevarer.*Indeholder positivliste over monomere udgangsstoffer og additiver, samt specifikationer for visse af stofferne. http://eur-lex.europa.eu/legal-content/DA/TXT/PDF/?uri=CELEX:02011R0010-20150226&qid=1428414133322&from=DA. Fortolkning af phthalatreglerne i forordning 10/2011: https://www.foedevarestyrelsen.dk/SiteCollectionDocuments/25_PDF_word_filer%20til%20download/06kontor/FKM/phthalatregler-fortolkning-2012.pdf

Grænseværdier for bly og cadmium i keramik og emaljerede genstande, samt glasvarer: Bekendtgørelse nr. 822 af 26/06/2013 om fødevarekontaktmaterialer. https://www.retsinformation.dk/Forms/R0710.aspx?id=152320

For øvrige metaller, samt revision af bly og cadmium-grænserne, se Europarådets guide: Council of Europe/EDQM: Metals and alloys used in food contact materials and articles. A practical guide for manufacturers and regulators. 2013.

Contaminants in food: COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (consolidated version). Grænser for bly, cadmium og kviksølv, dioxiner, PCB m.fl. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1881-20160311&qid=1464006829946&from=EN

[ii] **Cosmetics**

REGULATION (EC) No 1223/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 November 2009 on cosmetic products (consolidated)
Note, *article 15* prohibits/restricts the use of CMR substances in general (indicated as CMR-reg); *Annex II* specifically lists prohibited substances**.**

Toys
[iii] Danish Bekendtgørelse nr. 13 af 10/1-11 om sikkerhedskrav til legetøjsprodukter

restricts the use of CMR substances in toys in concentrations above the specific classification limit (indicated as CMR-reg).

[iv] **Biocides** Listen over biocidholdige aktivstoffer: http://echa.europa.eu/da/information-on-chemicals/biocidal-active-substances

Godkendte produkter: http://mst.dk/virksomhed-myndighed/bekaempelsesmidler/bekaempelsesmiddeldatabase/bmd/

[v] Soil and evaporation:

http://mst.dk/media/131857/kvalitetskriterier-jord-og-drikkevand-juni-2015.pdf

B- values:

http://www2.mst.dk/Udgiv/publikationer/2016/08/978-87-93529-02-1.pdf

Further foot notes

[vi] COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (consolidated version).
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1881-20160311&qid=1464006829946&from=EN

[vii] COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (consolidated version).
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1881-20160311&qid=1464006829946&from=EN

[viii] COMMISSION REGULATION (EC) No 1881/2006 of 19 December 2006 setting maximum levels for certain contaminants in foodstuffs (consolidated version).
http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02006R1881-20160311&qid=1464006829946&from=EN

[ix] Bekendtgørelse nr. 1217 af 11/10-2013 om forbud mod import, salg og anvendelse af visse parabener i kosmetiske produkter til børn under 3 år

[x] Bekendtgørelse nr. 1217 af 11/10-2013 om forbud mod import, salg og anvendelse af visse parabener i kosmetiske produkter til børn under 3 år

[xi] Grænserne varierer alt efter fødevarens beskaffenhed og om der er tale om enkelt eller flergangsbrug. Se nærmere her: https://www.foedevarestyrelsen.dk/SiteCollectionDocuments/25_PDF_word_filer%20til%20download/06kontor/FKM/phthalatregler-fortolkning-2012.pdf

[xii] Bekendtgørelse nr. 849 af 24/6-2014 om forbud mod ftalater i legetøj og småbørnsartikler.

Appendix 6a

Estimated Exposure, children < 3 years

(if not otherwise specified toddlers are children in the age of 1-3 years and infants < 1 year)

The tables below contain ***six columns***:

Selected references: indicating the literature found most relevant for exposure estimations (i.e. the references identified in appendix 3 with a scoring of ++ or +++ and further literature identified during the process for this more detailed exposure assessment).

Source of exposure: describe the specific exposure source(s).

Exposure: indicate the values of the exposure estimates given in the reference.

Further calculations/modifications: explains when further specific calculations or modifications of the data is necessary for the purpose of generation of exposure estimates for this project.

Mean exposure: in this column the *typical or mean/average exposure estimate* is given and the relevant exposure route is indicated. (Intern) is indicated if the internal dose (i.e. the systemic absorbed dose is indicated from the reference).

Worst-case/95 percent exposure: in this column, a *realistic worst case* or *95-percentile exposure estimate* is given and the relevant exposure route is indicated. (Intern) is indicated if the internal dose (i.e. the systemic absorbed dose is indicated from the reference).

Furthermore the tables contain a **Comment box** in which the further information, explanation or conclusions for the purpose of this project is given. Also, the tables contain a box for the indication and short discussion of available **human biomonitoring** (data from appendix 5c covering a table with the identified biomonitoring data).

Exposure estimates given in **bold** are the values that are considered most relevant for this project and the further risk assessment (i.e. these figures cover specifically the target groups of this projects (children below 3 years or unborn children/pregnant women), they are the most updated figures or the figures are considered most relevant for Danish conditions today).

NB: When specific calculations for background exposure of toddlers in relation to chemical content in drinking water, soil and air the following exposure parameters have been used for a 1-3 year old child with a bodyweight of 13 kg (Danish EPA 2006):

Mean and 95-percentile drinking water ingestion of 0.03 L/kg/d and 0.08L/kg/d
Mean and 95-percentile soil ingestion amount of 7.7 mg/kg/d and 15 mg/kg/d
Daily inhalation volume of air of 0.5 m3 air/kg/d

Antioxidants

BHA					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012	Food (as food additive) Food contact material Cosmetics	Toddlers Mean: 0.04-0.23 mg/kg bw/d High level (95-perc): 0.14-0.57 mg/kg bw/d Estimation for toddlers: 2.5 mg/kg bw/d The exposure through cosmetics was not considered relevant in small children		230 µg/kg bw/d (oral) (2500 µg/kg bw/d (oral))*	570 µg /kg bw/d (oral)
MEFD 2016	Drinking water Soil	**Limit value:** 0,5 µg/l **Limit value:** 70 mg/kg	0.03 L/kg/d water ingestion of toddlers (mean) 0.08 L/kg/d water ingestion of toddlers (95-perc) 7.7 mg/kg/d soil ingestion of toddlers (mean) 15 mg/kg/d soil ingestion of toddlers (95-perc)	0.015 µg/kg bw/d (oral) 0.539µg /kg/d (oral)	0.04 µg/kg bw/d (oral) 1.05 µg/kg/d (oral)
This project	Cosmetics Vitamin pills	Separate exposure estimations will be made in chapter 6 based on analytical data made during this project. Data from Danish manufacturers/ importers of vitamin pills indicate that the use of the substance			

		recently has been phased out (Danish Veterinary and Food Administration, personal cummunication2016). Thus, exposure from vitamin pills is not considered relevant.			
Aggregated exposure taken forward in evaluation (Food additive + contact materials):				**231 µg /kg bw/d (oral)**	**571 µg /kg bw/d (oral)**
Comments: The estimates of BHA exposure was based on dietary exposure. However, data are lacking from food contact materials. EFSA based their exposure estimates from food contact materials on the assumption that individuals consume 1 kg of food packed in plastics regardless of their age. *However, preliminary Danish data indicate no migration of BHA so exposure from FCM will not be considered further (Personal communication from the Danish Environmental and Food Agency 2016). Exposure from contaminated soil is considered to occur seldom and is therefore not included in the exposure estimate for risk assessment. Exposure calculated from research papers Mancini et al (2015) reach similar levels of exposure from food in French children. BHA was not found in the Danish database on consumer products**.**					
Human biomonitoring: No human biomonitoring study within the identified criteria were found.					

References

EFSA Journal 2012;10(7):2759. SCIENTIFIC OPINION Statement on the safety assessment of the exposure to butylated hydroxyanisole E 320 (BHA) by applying a new exposure assessment methodology.

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg

Mancini et al 2015. Dietary exposure to benzoates (E210–E213), parabens (E214–E219), nitrites (E249–E250), nitrates (E251–E252), BHA (E320), BHT (E321) and aspartame (E951) in children less than 3 years old in France. Food Additives & Contaminants: Part A, Vol. 32, No. 3, 293–306

BHT					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012	Food As food additive Food contact material Cosmetics	Children (3-9 years) Mean: 0.01-0.09 mg/kg bw/d High level (95-perc): 0.05-0.30 mg/kg bw/d Estimated for children (3-9 years): 0.2 mg/kg bw/d		**90 µg /kg bw/d (oral)** (200 µg /kg bw/d (oral))*	**300 µg /kg bw/d (oral)**
MEFD 2016	Drinking water Soil	**Limit value:** 0.5 µg/l **Limit value:** 70 mg/kg	0.03 L/kg/d water ingestion of toddlers (mean) 0.08 L/kg/d water ingestion of toddlers (95-perc) 7.7 mg/kg/d soil ingestion of toddlers (mean) 15 mg/kg/d soil ingestion of toddlers (95-perc)	0.015 µg/kg bw/d (oral) 0.539 µg/kg/d (oral)	0.04 µg/kg bw/d (oral) 1.05 µg/kg/d (oral)
Data Danish EPA database on consumer products	Consumer products for children i.e. diapers, ballons and facial paint	BHT was detected in the products but the exposure was not estimated			
This project	Cosmetics Vitamin pills	Separate exposure estimations, see chapter 6.6.1. Body lotion: 480 µg/kg bw/d (dermal), corresponding to 19.2 µg/kg bw/d (internal dose). Sunscreen and body lotion total: 2016 µg/kg bw/d (dermal), corresponding to 80.6 µg/kg bw/d (internal dose). Data from Danish manufacturers/ importers of vitamin pills indicate that the use of the substance recently has been phased out (Danish EPA communication 2016). Thus,		480 µg/kg bw/d (dermal), corresponding to **19.2 µg/kg bw/d (internal dose)**	2016 µg/kg bw/d (dermal), corresponding to **80.6 µg/kg bw/d (internal dose)**

		exposure from vitamin pills is not considered relevant.			
Aggregated exposure taken forward in evaluation:				**111 µg /kg bw/d (oral)**	**382 µg /kg bw/d (oral)**
Comments: The estimates on BHT exposure are lacking data from food contact materials. EFSA based their exposure estimates from food contact materials on the assumption that individuals consume 1 kg of food packed in plastics regardless of their age. *However, preliminary Danish data indicate no migration of BHTso exposure from FCM will not be considered further (Personal communication from the Danish Environmental and Food Agency 2016). BHT was measured in several consumer products relevant for small children. The exposure from these sources (e.g. diapers) may be relevant. However, at present no relevant exposure estimates are available.					
Human biomonitoring: No human biomonitoring study within the identified criteria were found.					

References

EFSA 2012: Scientific Opinion on the re-evaluation of butylated hydroxytoluene BHT (E 321) as a food additive. EFSA Journal 2012;10(3):2588

Danish EPA database on chemicals in consumer products: http://mst.dk/virksomhed-myndighed/kemikalier/fokus-paa-saerlige-produkter/database-over-kemiske-stoffer-i-forbrugerprodukter/

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Brominated compounds

HBCDD					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish DTU 2015	Food	**Children 4-14 years** Average: 0.23 ng/kg/d 95-perc: 1.28 ng/kg/d	For Danish toddlers a higher exposure than for 4-14 year old children would be expected. The data from EFSA for children above 1 years is used for the exposure estimate for toddlers.		
EFSA 2011a	Food	**Infant (breast-fed)** Average: 0.6 -142 ng/kg/d High:0.9- 213 ng/kg/d	Very broad range for infant exposure throughout Europe, and the high exposure levels seem unrealistic for Danish infants due to low exposure to the Danish adult population.		
	Food	**Children 1-14 years** Average: 1.06 ng/kg/d High level: 2.7 ng/kg/d		**0.0011 µg/kg/d (o)**	**0.0027 µg/kg/d (o)**
	Dust	Children 1-6 years (UK): Average: 5.9 ng/kg/d High: 330 ng/kg/d		**0.0059 µg/kg/d (o)**	**0.330 µg/kg/d (o)**
	Dust	Children (<1year) (Belgium) 0.67 ng/kg/d	Dust exposure seems highly variable.		
	Aggregate exposure food + dust:			**0.007 µg/kg/d (o)** **NB. dust contribution may vary considerable !**	**0.333 µg/kg/d (o)** **NB. dust contribution may vary considerable !**
TBBPA					
EFSA 2011b	Food	Toddlers, high consumption of cow milk: 55.7 ng/kg/d		-	**55.7 ng/kg/d**
	Dust	Toddlers Typical exposure: 1.2 ng/kg/d High exposure: 4.6 ng/kg/d		1.2 ng/kg/d	**4.6 ng/kg/d**

	Air	Child of 20 kg: High exposure: 0.023 ng/kg/d			
	Toddlers, aggregate high exposure			**No estimate**	**60 ng/kg/d:**
Deca-BDE (BDE-209)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2011c	Food	**Infants** Infants average: 0.013 µg/kg/d Infants high : 0.042 µg/kg/d		0.013 µg/kg/d (o)	0.042 µg/kg/d (o)
	Food	**Toddlers:** Toddlers, average: 0.010 µg/kg/d Toddlers, high: 0.018 µg/kg/d		**0.010 µg/kg/d (o)**	**0.018 µg/kg/d (o)**
	Dust	Toddlers, low: 0.0005 µg/kg/d Toddlers, high: 0.080 µg/kg/d		**0.0005 µg/kg/d (o)**	**0.080 µg/kg/d (o)**
	Toddlers, aggregate food+ dust:			**0.011 µg/kg/d (o)**	**0.098 µg/kg/d (o)**
Tetra + Penta-BDE (BDE-47 + BDE-99)					
EFSA 2011c	Food	**Infants (BDE-47 + BDE-99)** Infants av.: 0.018 + 0.007 µg/kg/d Infants high : 0.070 + 0.026 µg/kg/d	**Infants** BDE-47 BDE-99	**0.018 µg/kg/d** **0.007 µg/kg/d**	**0.070 µg/kg/d** **0.026 µg/kg/d**
		Toddlers: Toddlers av.: 0.006 + 0.003 µg/kg/d Toddlers, high: 0.016 + 0.006 µg/kg/d	**Toddlers** BDE-47 BDE-99	0.006 µg/kg/d 0.003 µg/kg/d	0.016 µg/kg/d 0.006 µg/kg/d
Hexa-BDE (BDE-153)					
EFSA 2011c	Food	**Infants:** Infants av.: 0.00088 µg/kg/d Infants high : 0.0022 µg/kg/d		0.00088 µg/kg/d	0.0022 µg/kg/d
		Toddlers: Toddlers av.: 0.0016 µg/kg/d Toddlers, high: 0.0032 µg/kg/d		**0.0016 µg/kg/d**	**0.0032 µg/kg/d**
Comments: For all the brominated flame retardants food is an important source for exposure of infants and toddlers. For HBCCD and Deca-PDE exposure through dust intake may dominate the overall exposure. For BDE-47 and BDE-99 a German study indicated that non-dietary exposure i.e. inhalation and dust ingestion accounted for 4-6% of the total exposure.					
Human biomonitoring: The levels of poly brominated flame retardants have been measured several times in Danish children and women. Widespread exposure to PBDEs is documented and exposure calculations were made for breastfed infants from measurements of BDE47 + BDE99 in human milk (Median (max): 0.009 µg/kg/d (0.1 µg/kg/d) and 0.003 µg/kg/d (0.043 µg/kg/d))					

References.

Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Kortlægning af kemiske stoffer i forbrugerprojekter nr. 117. Miljøstyrelsen.

Danish EPA (2014). Survey of brominated flame retardants. Part of the LOUS-review. Environmental Project No. 1536. Danish Environmental Protection Agency.

Danish DTU (2015). Chemical contaminants. Food monitoring 2004-2011. National Food Institute. Technical University of Denmark. Division of Food Chemistry
EFSA (2011a). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Hexabromocyclododecanes (HBCDDs) in Food. EFSA Journal 2011;9(7):2296. [118 pp.] doi:10.2903/j.efsa.2011.2296. Available online: www.efsa.europa.eu/efsajournal
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Schlumpf M, Kypke K, Wittassek M, Angerer J, Mascher H, Mascher D, Vökt C, Birchler M, Lichtensteiger W. Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere. 2010 Nov;81(10):1171-83.

Chlorinated compounds

PCB/TCDD					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
PCB total. Sum of 6 PCB indicators as reference for other congeners (PCB6): PCB-28,-52,-101,-138,-153,-180.					
EFSA 2012	Food	Infants (EU) (human milk not included): Mean: 7.2-11.0 ng/kg/d 95-perc: 17.7-35.4 ng/kg/d Toddlers (EU): Mean: 8.3-25.7 ng/kg/d 95-perc: 18.2-52.7 ng/kg/d Adult (DK): Mean: 5.4-**6.3 ng/kg/d** 95-perc: 10.8-**11.8 ng/kg/d**	Toddlers having the highest exposure. However rather broad EU ranges in exposure estimates making an estimate from these figures very uncertain. A valid estimate of the exposure of toddlers would be a **factor 2** higher that the adult exposure according to Danish EPA (2014).	**12.6 ng PCB6/kg/d (o)**	**23.6 ng PCB6/kg/d (o)**
Danish HMA 2013	Evaporation to indoor air from building materials	Limit values for total PCBs: 300-3 000 ng /m3 corresponding to 60-600 ng PCB6/m^3	Toddlers inhaling 0.5 m^3 air/kg/d (Danish EPA 2006)		**300 ng PCB6/kg/d (inh)**
Danish EPA 2009	Measurement of dust	Highest level of 2000 ng/g dust measured as PCB7 (very comparable to PCB6-levels)	Toddlers ingesting 3.8 or 7.5 mg dust/kg/d (half the values as soil ingestion values)		**15 ng PCB6/kg/d (o)**
	Aggregate typical exposure, food only Worst case exposure, food, inh + dust (from PCB in indoor env.)			**12.6 ng PCB6/kg/d (o)**	**38,6 (o); 300 ng/kg/d (inh)**
DL-PCBs + dioxins					
EFSA 2012	Food	Infants (EU) (human milk not included): Mean: 1.08-1.17 pg TCDD eqv/kg/d 95-perc: 3.0-5.9 pg TCDD eqv/kg/d Toddlers (EU): Mean: 1.54-2.54 pg TCDD eqv/kg/d 95-perc: 2.6-9.9 pg TCDD eqv/kg/d	Toddlers having the highest exposure. However rather broad EU ranges in exposure estimates making an estimate from these figures very uncertain.		

		Adult (DK): Mean: **1.06 pg TCDD eqv/kg/d** 95-perc: **2.3 pg TCDD eqv/kg/d**	A valid estimate of the exposure of toddlers would be a factor 2 higher that the adult exposure according to Danish EPA 2014.	**2.12 pg TCDD eqv/kg/d (o)**	**4.6 pg TCDD eqv/kg/d (o)**
Comments: The EFSA data is considered the best data for exposure estimation as estimation of exposure of the Danish population is based on monitoring results from 2008-2010. (The estimates given by the recent publication by DTU Food 2015 (figures not included in the table) was based on data from 2004-2011, i.e. older data may affect the exposure estimations). For both non-dioxin-like PCBs and dioxin-like PCBs and dioxins in general the primary exposure is from ingestion of food. For non-dioxin like PCBs a significant additional exposure that exceeds exposure from food may come from inhalation of indoor air contaminated with PCBs evaporated (i.e. dominated by the lower molecular weight PCBs congeners) from PCB-containing building materials (typically sealings).					
Human biomonitoring: Plasma concentrations of PCBs have been measured in Danish children and adults. The measurements show that the Danish population is still exposed to PCBs even though their use have been banned for many years. Further, the study of inhabitants of contaminated buildings show that indoor air may be an important source to PCB exposure, if living in buildings built with PCB-containing material. For breastfed infants, the intake of breastmilk is an important exposure source. Exposure calculations have been performed for Swiss infants based on the PCB concentrations measured in breast milk (**PCB7 median: 999 ng/kg/d, max: 2733 ng/kg bw/d)** Schlumpf 2010).					

References

Danish EPA (2009). Sundhedsmæssig vurdering af PCB-holdige bygningsfuger. Orientering fra Miljøstyrelsen Nr. 1 2009

Danish EPA (2014). Evaluation of health hazards by exposure to Polychlorinated biphenyls (PCB) and proposal of a health-based quality criterion for soil. Environmental Project No. 1485, 2014

Danish HMA (2013). HEALTH RISKS OF PCB IN THE INDOOR CLIMATE IN DENMARK – background for setting recommended action levels. Background report prepared for Danish Health and Medicines Authority by Nordic Institute of Sustainable Products and Environmental Chemistry and Toxicology

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. edition, juni 2015

EFSA (2012). SCIENTIFIC REPORT OF EFSA. Update of the monitoring of levels of dioxins and PCBs in food and feed. European Food Safety Authority. EFSA Journal 2012;10(7):2832.

Schlumpf et al. (2010). Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere. 2010 Nov;81(10):1171-83.

Tetrachloroethylene					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Indoor air; Indoor air + dry cleaned clothes	< 3 µg/m^3 in homes without known tetrachloroethylene sources 92 µg/m^3 as average level during 14 days after parents bringing tetrachloroethylene dry cleaned clothes home (small unvented flat).		**3 µg/m^3**	92 µg/m^3
MEFD 2015	Indoor air	100 µg/m^3 as regulatory limit value for migration of tetrachloroethyklen from a dry cleaning store to flats in the same building			**100 µg/m^3**
Comments: Exposures in relation to dry cleaning of clothes are considered the only significant exposures for consumers and the general population.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References:

Danish EPA (2016).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

MFED (2015). Bekendtgørelse nr 1457 af 07/12/2015 Bekendtgørelse om etablering og drift af renserier (Statutory order regarding the establishment and operation of dry cleanings stores). Ministry for Environment and Food of Denmark.

Trichloroethyl phosphate (TCEP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Total mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
SCHER 2009	Combined exposures From dermal contact to articles/ ingestion of dust	Exposure estimates (1-3 years), general /average external exposure: Routes of TCEP exposure — Exposure (µg/kg bw/d) Dermal contact (textiles, furniture, dust) — 12.12 House dust, typical exp. (including soil) — 0.1-0.7 Direct inhalation — 0.96 Drinking water — 0.01 **Total exposure** — **13.19-13.79** (When comparing to tolerable exposure levels the same absorption rate was used for all exposure routes).		**13.8 µg/kg bw/d (o+d+inh)**	-

	Toy: textile cube	Specific worse-case exposure from sucking a textile-cube: 240 µg/kg bw/d (no longer relevant –removed from market)		240 µg/kg bw/d (o)
Danish EPA 2015	Baby slings:	Oral: 1.85 x 10^{-2} mg/ kg bw/d (external and internal exposure) Dermal: 0.11 mg/kg bw/d (external exposure) 0.054 mg/kg/d (internal exposure, using 50% for dermal absorption)		**18.5 µg/kg bw/d (o and internal))** **54 µg/kg bw/d internal) =** **72.5 µg/kg bw/d (internal)**
Comments: The baby sling exposure estimate is considered uncertain and only apply to one specific scenario. In general the probability for exposure from articles today has been reduced as the use of TCEP in Europe is subjected to authorization under REACH.				
Human biomonitoring: No human biomonitoring study within the identified criteria was found.				

References

Danish EPA (2015). Chemical substances in car safety seats and other textile products for children. Survey of chemical substances in consumer products No. 135, 2015

SCHER (2012). SCHER (Scientific Committee on Health and Environmental Risks), Opinion on tris(2-chloroethyl)phosphate TCEP in Toys, 22 March 2012

Fluorinated compounds

PFAS					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
PFOA					
Livsmedelsverket 2013	Food	Children 2 years Average: 3.26 ng/kg/d 95-perc.: 4.84 ng/kg/d	Based on Swedish data	**3.26 ng/kg/d (o)**	**4.84 ng/kg/d (o)**
EFSA	Food	Infants Average: 0.16-11ng/kg/d 95-perc.: 0.46-15 ng/kg/d)	Based from data from EU countries		
		Toddlers Average: 0.28-10ng/kg/d 95-perc.: 0.58-14 ng/kg/d			**14 ng/kg/d (o)** **(worst case)**
Haug et al. 2011	Dust	Infants (½ year) Ingestion of 100 mg dust/d: 0.33 ng/kg/d Ingestion of 200 mg dust/d: 0.66 ng/kg/d	Norwegian data on dust content	**0.33 ng/kg/d (o)**	**0.66 ng/kg/d**
	Air	Medium, air: 0.049 ng/kg/d High scenario: 0.17 ng/kg/d	Norwegian data on air content	**0.049 ng/kg/d (inh)**	**0.17 ng/kg/d (inh)**
	Aggregate exposure food, dust, air (anticipating same absorption rate for oral and inh exposure)			**3.64 ng/kg/d**	**5.67 ng/kg/d**
PFOS					
Livsmedelsverket 2013	Food	Children 2 years Average: 1.31 ng/kg/d 95-perc.: 3.39 ng/kg/d	Based on Swedish data	**1.31 ng/kg/d (o)**	**3.39 ng/kg/d (o)**
EFSA	Food	Infants Average: 0.29-11ng/kg/d 95-perc.: 0.7-12 ng/kg/d	Based from data from EU countries		**13 ng/kg/d** **(wort case)**
		Toddlers Average: 1.2-8.5 ng/kg/d 95-perc.: 4.6-13 ng/kg/d			
Haug et al. 2011	Dust	Infants (½ year)	Norwegian data on dust content	**0.04 ng/kg/d (o)**	**0.09 ng/kg/d (o)**

	Air	Ingestion of 100 mg dust/d: 0.04 ng/kg/d Ingestion of 200 mg dust/d: 0.09 ng/kg/d Medium, air: 0.060 ng/kg/d High scenario : 0.30 ng/kg/d	Norwegian data on air content	**0.060 ng/kg/d (inh)**	**0.30 ng/kg/d (inh)**
	Aggregate exposure food, dust, air (anticipating same absorption rate for oral and inh exposure)			**1.41 ng/kg/d**	**3.78 ng/kg/d**
PFHxS					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Livsmedelsverket 2013	Food	Children Average: 0.16 ng/kg/d 95-perc.: 0.24 ng/kg/d	Based on Swedish data	**0.16 ng/kg/d**	**0.24 ng/kg/d**
EFSA 2012	Food	No estimates given due to few data			
Comments: Preference is given to data from the Nordic countries. Worst case scenario is, however, based on estimates from EFSA on data from all EU countries. For the 95-perc scenarios the content of PFOS and PFOA in air and dust found in the study by Haug et al. 2011 may contribute to less than 10% compared to the 95-perctile dietary exposure.					
Human biomonitoring: The plasma concentrations of PFASs have been measured in several Danish studies of pregnant women, non-pregnant women and children. Exposure calculations have not been performed from the serum/plasma levels, but the PFAS was detected in nearly all samples indicating widespread exposure. Based on the PFOS concentrations measured in **breast milk** in Germany an estimation of the daily exposure to PFOS in **infants** was made (**median 0.02 µg/kg bw/d, max: 0.054 µg/kg bw/d**, Völkel (2008)), indicating much higher exposure than infants not feed with mother´s milk (these values will be further used in the evaluation. Jensen (2015) and Mørck (2015) showed that women with several children have lower serum levels, which indicates that pregnancy and likely also breastfeeding status affects the PFAS levels in the blood.					

References

EFSA (2012). SCIENTIFIC REPORT OF EFSA. Perfluoroalkylated substances in food: occurrence and dietary exposure. European Food Safety Authority. EFSA Journal 2012;10(6):2743

Haug et al. (2011).Characterisation of human exposure pathways to perfluorinated compounds--comparing exposure estimates with biomarkers of exposure. Environ Int. 2011 May; 37(4):687-93.

Livsmedelsverket (2013). Riskvärdering av perfluorerande alkylsyror i livsmedel och dricksvatten. Rapport 11-2013.

Völkel et al., (2008) Perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA) in human breast milk: Results of a pilot study. Int. J. Hyg. Environ.-Health 211 (2008) 440–446

Hydrocarbons

Toluene					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data on indoor + outdoor+ microenvironments): Mean: 11.7 µg/m^3 95-perct: 55.3 µg/m^3	Used for 95-perc. "back-ground level"		**55.3 µg/m^3 (inh)**
	Indoor air	Average level 9.1 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**9.1µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	Indoor level of 230 µg/m^3 due to migration of gasoline vapour because of lawn-mover gasoline stored outside in a shed.	Specific worse-case scenario		**230 µg/m^3 (inh)**
Xylenes					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (Eu data on indoor + outdoor+ microenvironments): Mean: 6.7 µg/m^3 95-perct: 42.3 µg/m^3	Used for 95-perc. "back-ground level"		**42.3 µg/m^3 (inh)**
	Indoor air	Average level 7.5 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**7.5 µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	Evaporation from stored gasoline outside in a shed. 146 µg/m^3	Specific worse-case scenario		**146 µg/m^3 (inh)**
Ethylbenzene					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data indoor + outdoor+ microenvironments): Mean: 1.8 µg/m^3 95-perct: 8.2 µg/m^3	Used for 95-perc. "back-ground level"		**8.2 µg/m^3 (inh)**

	Indoor air	Average level 3.2 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**3.2 µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	Evaporation from stored gasoline outside in shed. 37 µg/m^3	Specific worse-case scenario		**37 µg/m^3 (inh)**
Total C6-C12, alifatic, alicyclic and aromatic hydrocarbons					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data indoor + outdoor+ microenvironments): Mean: 79 µg/m^3 95-perct: 232 µg/m3	Used for 95-perc. "back-ground level"	**79 µg/m^3 (inh)**	**232 µg/m^3 (inh)**
	Indoor air due to storage of gasoline	Evaporation from stored gasoline outside in shed. 1500 µg/m^3 (measured as TVOC)	Specific worse-case scenario		1500 µg/m^3 (inh)
	Indoor air	Average level < 338 µg/m^3 (measured as TVOC) measured in children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level		
Styrene					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (indoor + outdoor+ microenvironments): Mean: 0 µg/m^3 95-perct: 2.5 µg/m3	Used for 95-perc. "back-ground level"		**2.5 µg/m^3 (inh)**
	Food	Exposure to toddlers assumed to 6 µg/day from food and water (however considered very uncertain)			
Comments: Data from portable measuring devices are used as these figures typically indicate higher exposure compared to the estimated combined exposure from ambient air, indoor air and					

air inside cars. These data are pooled from measurements in 11 European cities and may most likely overestimate Danish conditions. Danish EPA (2016) examined evaporation from building materials, furniture, electronics and toys relevant for children and children´s rooms, however, only very low hydrocarbon levels were measured. Thus, laboratory measurements of these articles and also measurement of a children´s room mock-up clearly underestimated exposure in real life (performed in 19 homes).
Human biomonitoring: No human biomonitoring study within the identified criteria were found.

References

Danish EPA 2016).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

Danish-LOUS (2014a). Survey of white spirit. Environmental Project No. 1546. Part of the LOUS-review. Danish Environmental Protection Agency.

Danish-LOUS (2014b). Survey of styrene. Environmental Project No. 1612. Part of the LOUS-review. Danish Environmental Protection Agency.

Medicine

Paracetamol					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish medicines agency	Medicine	Recommended dose children (2-11 years): 50 mg/kg bw/d divided in 3-4 doses. Mean exposure scenario: 1 dose of 12.5 mg/kg bw/d Maximum exposure: Full dose of 50 mg/kg bw/d	Recommended dose 50 mg/kg bw/d divided in 3-4 doses for a maximum of 3 consecutive days without consulting a doctor	12.5 mg/kg bw/d (o)	50 mg/kg bw/d (o)
Comments: It is evident from the research paper listed in table 3.1 under paracetamol, that the medication of small children with paracetamol is quite common. The estimation of paracetamol exposure is based on the recommended intake of the paracetamol containing medication, panodil. When evaluating the risk of paracetamol exposure, it must be taken into consideration that the exposure is based on self-medication by the guardians of the children, and the exposure will occur in intervals. Furthermore the benefits of the medication must be taken into consideration.					
Human biomonitoring: The urinary excretion of paracetamol has been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that paracetamol could be detected in nearly all samples. The concentration of paracetamol in the urine was not always dependent on the intake of paracetamol medication and the authors suggests other sources of paracetamol e.g. from the metabolism of the chemical aniline which is present in the diet					

References: Product summary of Panodil (paracetamol medication) from Danish Medicines Agency. Retrieved on 04.07.2016

Metalic compounds

Aluminium					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
NSCFS 2013 and SCCS 2014 (identical values)	Food Cosmetics	Mean exposure, food: Children, 1year: 0.89 mg/kg bw/week 95-percentiles, food: Children, 1 year: 1.9 mg/kg bw/week As intake exposures. Oral bioavailability of 0,1 % is to be used for calculation of internal exposure. Children, 1 year: 0 mg/kg bw/week (cosmetics containing Al not considered relevant)	Only food exposure considered relevant for children ≤ 3years. Exposure converted to daily exposure	130 µg/kg/d (o)	270 µg/kg/d (o)
MEFD 2016	Drinking water	Limit value: 200 µg/L	0,03 L/kg/d water ingestion of toddlers (mean) 0.08 L/kg/d water ingestion of toddlers (95-perc)	6 µg/kg/d (o)	16 µg/kg/d (o)
Aggregated exposure taken forward in evaluation (food + drinking water):				**136 µg/kg/d (o)** **0.14 µg/kg/d (internal)**	**286 µg/kg/d (o)** **0.29 µg/kg/d (internal)**
Comments: No other relevant exposure could be found. The exposure estimates are considered reliable and given as internal dose levels using an oral absorption factor of 0.1%. However, some uncertainty apply to this figure. Further, there may be exposure to aluminium from its use in vaccines, that may contain up to about 1 mg of aluminium (Oxford University 2016).					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Oxford Universtity 2016.. http://vk.ovg.ox.ac.uk/vaccine-ingredients

NSCFS (2013). Risk assessment of the exposure to aluminium through food and the use of cosmetic products in the Norwegian population. Norwegian Scientific Committee for food safety. VKM- 05/04/2013

SCCS (2014). OPINION ON the safety of aluminium in cosmetic products. Scientific Committee on Consumer Safety. Revision of 18 June 2014

Lead					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012	Food	Total dietary exposure (mean): Infants: 0.73-1.09 µg/kg/d Toddlers: 0.87-1.18 µg/kg/d Total dietary exposure (95-perc.): Infants: 1.39-2.22 µg/kg/d Toddlers: 1.95-2.56 µg/kg/d	Toddlers most heavily exposed. Upper level of exposure interval chosen.	**1.18 µg/kg/d (o)**	**2.56 µg/kg/d (o)**
MST-LOUS 2014 MEFD 2016	Drinking water Soil Dust	Drinking water, average conc. of 0.9 µ/L : Children 2 years: 0.027 / 0.072 µg/kg/d (mean/worst case) Drinking water, high level at limit value of 10 µ/L: Children 2 years: 0.3/ 0.8 µg/kg/d (mean/ worst case) Soil, at quality criteria of 40 mg/kg: Children 2 years: 0.3/ 0.6 µg/kg/d (mean/ worst case) Soil, at typical levels in urban areas of 200 mg/kg: Children 2 years: 1.5/ 3 µg/kg/d (mean/ worst case) Dust: Children 2 years: 0.6 µg/kg/d	Used for both mean and worst-case exposure	**0.027 µg/kg/d (o)** 0.3 µg/kg/d (o) **0.3 µg/kg/d (o)** 1.5 µg/kg/d (o) **0.6 µg/kg/d (o)**	0.072µg/kg/d (o) **0.8 µg/kg/d (o)** 0.6 µg/kg/d (o) **3 µg/kg/d (o)** **0.6 µg/kg/d (o)**
	Aggregate mean exposure, drinking water content of 0.9 µg/L and soil content of 40 mg/kg **Aggregate worst case, drinking water content of 10 µg/L and soil content of 200 mg/kg**			**2.11 µg/kg/d (o)**	**6.96 µg/kg/d (o)**
ECHA/RAC 2014	articles	Exposure estimates based on mouthing behavior of metallic objects: Infants (½-1year) Realistic: 0.01 – 1.5 µg/kg/d Worst-case: 0.06 – 6.2 µg/kg/d	Using mouthing of object with a content of 3% a toddler would be exposed to 0.45 **µg/kg/d when mouthing for**		

		Toddlers (1-3 year) Realistic: 0.008 – 1.2 µg/kg/d Worst-case: 0.084 – 9.0 µg/kg/d The upper ranges of the values represent mouthing of an object with a lead content of 6%.	**15 min/d or 4.6 µg/kg/d when mouthing for 120 min/d**	**0.45 µg/kg/d (o)**	**4.6 µg/kg/d (o)**
Aggregate mean exposure, drinking water content of 0.9 µg/L and soil content of 40 mg/kg, dust and articles				**2.56 µg/kg/d (o)**	
Aggregate worst case, drinking water content of 10 µg/L and soil content of 200 mg/kg, dust and articles					**11.6 µg/kg/d (o)**
Comments: The exposure estimates are considered reliable, however, they are based on EU data (and not specifically Danish data) on lead content in food. Exposure from various articles that may be mouthed may constitute a very significant exposure to lead for toddlers.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

Danish EPA-LOUS (2014). Survey of lead and lead compounds. Environmental Project No. 1539. Part of the LOUS-review. Danish Environmental Protection Agency.

ECHA/RAC (2014). Background document to the Opinion on the Annex XV dossier proposing restrictions on Lead and its compounds in articles intended for consumer use. ECHA/RAC/RES-O-0000003487-67-04/F.ECHA/SEAC/ RES-O-0000003487-67-05/F. 7. April 2014.

EFSA (2012) SCIENTIFIC REPORT OF EFSA. Lead dietary exposure in the European population. European Food Safety Authority. EFSA Journal 2012;10(7):2831

Mercury					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Inorganic mercury					
EFSA 2012	Food	***Inorganic mercury:*** Median dietary exposure (median level derived from various country mean levels) Toddlers: 1.13 µg Hg/kg/week 95-percentile values (median levels of various county 95-percentile levels) Toddlers: 1.62 µg Hg/kg/week	Converted to daily exposure	**0.16 µg Hg/kg/d (o)**	**0.23 µg Hg/kg/d (o)**
MEFD 2016	Drinking water	**Inorganic mercury** At limit value of 1 µg/L		**0.03 Hg/kg/d (o)**	**0.08 Hg/kg/d (o)**
	Aggregated exposure at drinking water content of 1 µg/L			**0.19 Hg/kg/d (o)**	**0.31 Hg/kg/d (o)**
SCHER 2010	Energy saving light bulbs	7-year old child: Scenario 1 without venting: 10 µg/kg bw for 2 days Scenario 2 with immediate venting: 0.6 µg/kg bw/d for one day (calculated as internal doses using a lung absorption of 80%)	This sourec of exposure evalauted separately		Scenario 1 **10 µg/kg bw/d** for 2 days (internal dose) Scenario 2 **0.6 µg/kg bw/**d for 1 day

Methylmercury:					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012		***Methylmercury:*** Median dietary exposure (median level derived from various country mean levels) Toddlers: 0.27 µg Hg/kg/week (95-percentile values (median levels of various county 95-percentile levels): Toddlers: 1.59 µg Hg/kg/week	Converted to daily exposure	**0.039 µg Hg/kg/d (o)**	**0.23 µg Hg/kg/d (o)**
Aggregated exposure: only data from exposure from food				**0.039 µg Hg/kg/d (o)**	**0.23 µg Hg/kg/d (o)**
Comments: The exposure estimates are considered reliable, however, they are based on surveys on toddlers from other European countries. Possible exposure to mercury from its use as preservative in vaccines (Thiomersal / ethyl-mercury) may be a further source of exposure. About 25µ Hg/dose (Netdoktor 2016).					
Human biomonitoring: The levels of mercury have been measured the hair of Danish children and their mothers. Exposure calculations have not been performed, but the intake of fish was significantly associated mercury concentrations in hair (Mørck 2015a).					

References

EFSA (2012). Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal 2012;10(12):2985

Mørck et al (2015a). The Danish contribution to the European DEMOCOPHES project: A description of cadmium, cotinine and mercury levels in Danish mother-child pairs and the perspectives of supplementary sampling and measurements. Environmental Research 141 (2015) 96–105

SCHER (2010). Opinion on Mercury in certain Energy-saving Light Bulbs – Exposure of Children Scientific Committee on Health and Environmental Risks. The SCHER adopted this opinion at its 16th plenary on 22 March 2012

Parabens

Propylparaben (PP) + Butylparaben (BP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
SCCS 2013	Cosmetics	3-months old infant: 0.0408mg*/kg bw/day (int) Using a dermal absorption rate of 3.7% And assuming a content of 0.19% of propyl- + butylparaben in all leave-on products using 3 g/d. *sum of propyl- and butylparaben	Considered by SCCS as a worst case that all cosmetics applied contain propyl- and butylparaben		0.0408mg*/kg bw/day (int) *sum of propyl- and butylparaben Dermal abs of 3.7%
Danish EPA 2009	Cosmetics	Toddlers, cosmetics (without sunscreen): 0.144 mg/kg/d (int) with a content of 0.4% PP or BP and a dermal absorption factor of 10% Worst case exposure : 0.454 mg/kg/d (int) 18 g sunscreen twice a day with a content of 0.4% PP or BP and a dermal absorption factor of 10%	The daily scenario without sunscreen is taken as typical (mean) exposure, whereas days using 36 g of sunscreen (as only cosmetic) is taken as a worst case scenario.	0.144 mg/kg/d (int) dermal abs of 10% corresponding to **0.0533 mg/kg/d (int)** **with abs rate of 3.7%** see further adjustment below	0.454 mg/kg/d (int) dermal abs of 10% corresponding to **0.168mg/kg/d (int)** **with abs rate of 3.7%** see further adjustment below
Comments: It should, however, be noted that use of PP and BP is not allowed in cosmetic products intended to children below 3 years. The Danish EPA´s exposure estimations for daily use of cosmetic (sunscreens and other cosmetics are chosen for the exposure scenarios for toddlers, however corrected by the absorption factor concluded by SCCS 2013 and considering that cosmetics intended for older age groups containing PB and BB is used. **Further , the values in the table is calculated with a content of PB+BB of 0.4%, however, today a maximum level of 0.14% for PB + BB has been implemented and the exposure values should therefore be reduced by a factor 0.14%/0.4% i.e. to a mean exposure of 0.019 mg/kg/d (int) and a worst case exposure of 0.059 mg/kg/d (int)**					
Human biomonitoring: Comments: The paraben concentrations of propyl- and butylparaben along with methyl- and ethylparabens, have been measured several Danish studies of Danish children adult women/pregnant women. The measurements show that the detection of propyl- and butylparaben in the urine of Danish children and women are generally lower compared to the shorter chained parabens methyl- and ethylparaben. Further the measurements show that the highest exposure to parabens is among the youngest children and women. Exposure calculations have been performed for infants based on levels measured in breast milk from Swiss mothers (median: 301.3 ng/kg bw/d, max: 381.1 ng/kg bw day), but no exposure calculations were performed for adults Schlumpf (2010).					

References:

Danish EPA 2009. 2-åriges udsættelse for kemiske stoffer. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 103, 2009.
SCCS 2013: Scientific Committee on Consumer Safety SCCS/1514/13. OPINION ON Parabens.
Schlumpf (2010). Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor, pesticides, PBDEs, and PCBs in human milk: Correlation of UV filters with use of cosmetics. Chemosphere 81 (2010) 1171–1183

Pesticides

Pesticides					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Jensen et al. 2015	Food	**Adults (men+women) (µg/kg bw/day):** Diazinon 0.0047 Pirimiphos-methyl 0.043 Dicofol (sum) 0.017 Procymidone 0.018 Dimethoate 0.0063 Carbaryl 0.043 Chlorfenvinphos 0.0028 Carbendazim and benomyl 0.087 Dithiocarbamates 0.21 Linuron 0.010 Methomyl and thiodicarb 0.0083 Methamidophos 0.0029 Imazalil 0.072 Oxydemeton-methyl (sum) 0.00074	Compared to a total pesticide exposure of 1.9 µg/kg bw/day for adults, children (4-6 years) are exposed to 4.5 µg/kg bw/day **I.e., in average the figures for the speicifc pesticieds may be corrected with a factor 4.5/1.9 = 2.37 for children with an average consumption of fruit and vegetables.** As no data for toddlers are given the figures for children (4-6 years) will be used for toddlers as well. No high consumptions scenario for children was given.	**Toddlers (µg/kg bw/day)** **Diazinon 0.011** **Pirimiphos-methyl 0.10** **Dicofol (sum) 0.040** **Procymidone 0.043** **Dimethoate 0.015** **Carbaryl 0.10** **Chlorfenvinphos 0.0066** **Carbendazim and benomyl 0.20** **Dithiocarbamates 0.50** **Linuron 0.024** **Methomyl and thiodicarb 0.020** **Methamidophos 0.0069** **Imazalil 0.17** **Oxydemeton-methyl (sum) 0.0018**	Only data regarding average exposure included in the data by Jensen et al. 2015.
Comments: For exposure calculation of the pesticides the Danish exposure figures from the recent publication of Jensen et al. (2015) are used.					
Human biomonitoring: The urinary excretion of dialkylphosphates, with are metabolites of organophosphate pesticides such as Chlorpyrifos, have been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that the organophosphate metabolites could be detected in nearly all samples.					

References:

Jensen BH, Petersen A, Nielsen E, Christensen T, Poulsen ME, Andersen JH. Cumulative dietary exposure of the population of Denmark to pesticides. Food Chem Toxicol. 2015 Sep; 83: 300-7.

Phenolic compounds

Bisphenol A					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2011	Pacifier	Infant (worst case): 0.00023 mg/kg/d (o) In connection with 7.75 hours of use of the pacifier and a Bisphenol A migration rate of 0,019 µg/cm2/h			**230 ng/kg/d (o)**
EFSA 2015b	Food Dust Toys Pacifiers Articles that may be mouthed	Food (oral): Infants: Mean: 375 ng/kg/bw d Max: 857 ng/kg/bw/d Toddlers: Mean: 375 ng/kg/bw d Max: 857 ng/kg/bw/d Total (oral food + dust + toy + inh + dermal) Infants: Mean: 387 ng/kg/bw d Max: 878 ng/kg/bw/d Toddlers: Mean: 384 ng/kg/bw d Max: 870 ng/kg/bw/d For internal exposure the oral and the inhalational absorption rates were assumed to be 100% while dermal absorption from cosmteics was set to 50%		**375 ng/kg/bw d** 375 ng/kg/bw d **387 ng/kg/bw d (int)** 384 ng/kg/bw d	**857 ng/kg/bw/d** 857 ng/kg/bw/d **878 ng/kg/bw/d (int)** 870 ng/kg/bw/d
Aggregated oral exposure of infants taken forward in evaluation, for the special scenario estimates the Danish EPA exposure estimate on pacifiers is included:				**387 ng/kg/bw d (o)**	**878 ng/kg/bw d (o)**
Comments: The data from EFSA 2015 updated data of high quality and the total exposure estimates are based on these data. Aggregate exposure considered highest for infants. In the Danish database on consumer product many products containing bisphenol A are found, with the highest exposure potential from baby dummies/pacifiers and thermal paper.					
Human biomonitoring: Bisphenol A has been measured several times in Danish children and women and widespread exposure is documented. Exposure calculations has been made to estimate the exposure levels. The calculated exposure levels are similar to or lower compared to the estimated exposure presented in the present table: Mean: 0.04-0.066 µg/kg bw/d, 96-perc:					

0.15-0.283 µg/kg bw/d (Frederiksen 2013a+b). However, it must be mentioned that the biomonitoring studies were performed on children older than 6 years of age and therefore certain exposure sources specific for the babies and toddlers such as pacifiers are not reflected by these studies. EFSA 2015 noted by comparing estimated internal exposure with biomonitoring data, the forward modelling approach gave about 4-fold higher estimates (42–387 vs. <10–107 ng/kg bw per day) than the biomonitoring approach for average exposure, and about 2-fold higher for high exposure, demonstrating quite a good agreement between these two approaches.

References:

Danish EPA 2011: Undersøgelse af afgivelse af bisphenol A fra kasseboner og narresutter. Kortlægning af kemiske stoffer i forbrugerprodukter Nr. 110 2011.
EFSA 2015: Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids. EFSA Journal 2015;13(1):3978
Frederiksen et al., 2013a. Bisphenol A and other phenols in urine from Danish children and adolescents analyzed by isotope diluted TurboFlow-LC-MS/MS. Int J Hyg Environ Health. 2013 Nov;216(6):710-20.
Frederiksen et al., 2013b. Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. 2013 Nov;216(6):772-83.

Bisphenol F

Selected References	Source of exposure	Exposure	Further calculations/ modifications	Mean exposure (oral, dermal, inhal, intern)	Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)
Liao 2013	Food Based on measurements of beverages, dairy products, fats and oils, fish and seafood, cereals, meat and meat products, fruits, vegetables and others Paper	Dietary intake Infants (<1 year): Mean: 12.9 ng/kg bw/d 95-perc: 32.1 ng/kg bw/ d Toddlers (1-6 years) Mean: 22.3 ng/kg bw/d 95-perc: 70.3 ng/kg bw/d		12.9 ng/kg bw/d (o) **22.3 ng/kg bw/d (o)**	32.1 ng/kg bw/d (o) **70.3 ng/kg bw/d (o)**
Aggregated exposure of toddlers taken forward in evaluation:				**22.3 ng/kg bw/d (o)**	**70.3 ng/kg bw/d (o)**
Comments: The exposure estimates for Bisphenol F are based on the exposure estimates from an American research paper, with US measurements. All though there may be continental differences, the estimated exposures are considered relevant for the present project as more local data are missing.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References:

Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. Agric Food Chem. 2013 May 15;61(19):4655-62

Bisphenol S					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Liao 2013	Food Based on measurements of beverages, dairy products, fats and oils, fish and seafood, cereals, meat and meat products, fruits, vegetables and others	Dietary intake Infants (<1 year): Mean: 1.71 ng/kg bw/d 95-perc: 1.97 ng/kg bw/ d Toddlers (1-6 years) Mean: 4.34 ng/kg bw/d 95-perc: 4.74 ng/kg bw/d		1.71 ng/kg bw/d (o) **4.34 ng/kg bw/d (o)**	1.97 ng/kg bw/d (o) **4.74 ng/kg bw/d (o)**
Aggregated exposure of toddlers taken forward in evaluation:				**4.34 ng/kg bw/d (o)**	**4.74 ng/kg bw/d (o)**
Comments: The exposure estimates for Bisphenol S are based on the exposure estimates from an American research paper, with US measurements. All though there may be continental differences, the estimated exposures are considered relevant for the present project as more local data are missing.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References:

Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. Agric Food Chem. 2013 May 15;61(19):4655-62.

Nonylphenol					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
MEFD 2016	Drinking water	Limit values: Drinking water: 20 µg/l	0.03 L/kg/d water ingestion of toddlers (mean) 0.08 L/kg/d water ingestion of toddlers (95-perc)	**0.6 µg/kg bw/d (o)**	**1.6 µg/kg bw/d (o)**
		Soil: 25 mg/kg	7.7 mg/kg/d soil ingestion of toddlers (mean) 15 mg/kg/d soil ingestion of toddlers (95-perc)	**0.193 µg/kg bw/d (o)**	**0.375 µg/kg bw/d (o)**
Aggregated exposure taken forward in evaluation :				**0.79 µg/kg bw/d (o)**	**1.98 µg/kg bw/d (o)**
Comments: No data found regarding exposure from food and consumer products. The exposure to nonylphenol in children based on the consumption of drinking water and soil can be estimated. It may be noted, however, that the estimates of the exposure in adults from the MST 2012a report on pregnant women, found significant exposure from consumer products such as clothing.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References.

MST 2012a: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Phthalates

DEHP (di-ethyl-hexyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Bekö et al. 2013	Indoor air and dust (estimated) and total exposure (biomonitoring)	Measurement of phthalates in dust samples from **500 Danish homes and 150 day care centers.** Dermal exposure, inhalation exposure and ingestion through dust was estimated for the **children (3-6 years). Urine samples were taken from 431 children and analysed.**	These data for 3-6 years old children are considered realistic **for toddlers** as well.		
		Indoor exp (calculated based on dust content) Children 3-6 years (internal dose): Median: 0.83 µg/kg/d 95-perc.: 3.07 µg/kg/d Max: 9.69 µg/kg/d	Indoor dust/air	0.83 µg/kg/d (int)	3.07 µg/kg/d (int)
		Other exposure (food + articles), estimated as difference between biomonitoring in urine and estimated contribution from indoor env: Children 3-6 years (internal dose): Median: 3.94 µg/kg/d 95-perc.: 16.6 µg/kg/d Max: 533 µg/kg/d	Other exposure, food, articles, indoor environment? etc.	3.94 µg/kg/d (int)	16.6 µg/kg/d (int)
			Sum, Danish data (biomonitoring)	**4.77 µg/kg/d (int)**	**19.7 µg/kg/d (int)**
ECHA2016	Various articles Indoor env. Food	I**nfants** (6-12 months) Articles: Median: 3.49 µg/kg/d Worst case: 27.32 µg/kg/d	Articles	**3.49 µg/kg/d (int)**	**27.32 µg/kg/d (int)**
		Indoor env.: Median: 4.22 µg/kg/d Worst case: 21.85 µg/kg/d	Indoor env.	**4.22 µg/kg/d (int)**	**21.85 µg/kg/d (int)**
		Food: Median: 4.66 µg/kg/d Worst Case: 7.09 µg/kg/d	Food	**4.66 µg/kg/d (int)**	**7.09 µg/kg/d (int)**

		No data on toddlers in ECHA (2016) but only on older children (6-11 years) which is not considered relevant for this project.	Sum, EU data	**12.37 µg/kg/d (int)**	**56.26 µg/kg/d (int)**
DBP (di-butyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Bekö et al. 2013	Indoor air and dust (estimated) and total exposure (biomonitoring)	Measurement of phthalates in dust (see above) Indoor exp (calculated based on dust content)	Data for 3-6 years old children considered realistic for **toddlers** as well.		
		Children 3-6 years (internal dose): Median: 0.97 µg/kg/d 95-perc.: 3.50 µg/kg/d Max: 10.1 µg/kg/d	Indoor dust/air	0.97 µg/kg/d (int)	3.50 µg/kg/d (int)
		Other exposure (food + articles): Children 3-6 years (internal dose): Median: 2.59 µg/kg/d 95-perc.: 9.56 µg/kg/d Max: 163 µg/kg/d	Other exposure, food, articles etc.	2.59 µg/kg/d (int)	9.56 µg/kg/d (int)
			Sum Danish data, biomonitoring	**3.56 µg/kg/d** (int)	**13.06 µg/kg/d (int)**
ECHA 2016	Various articles Indoor env. Food	**Infants** (6-12 months) Articles: Median: 1.20 µg/kg/d Worst case: 9.22 µg/kg/d	Articles	**1.20 µg/kg/d**	**9.22 µg/kg/d**
		Indoor env.: Median: 0.28 µg/kg/d Worst case: 1.47 µg/kg/d	Indoor env.	**0.28 µg/kg/d (int)**	**1.47 µg/kg/d (int)**
		Toddlers, food: Median: 0.70 µg/kg/d (int) Worst casw:: 1.24 µg/kg/d	Food	**0.70 µg/kg/d (int)**	**1.24 µg/kg/d (int)**
			Sum EU data:	**2.18 µg/kg/d (int)**	**11.93 µg/kg/d (int)**

		No data on toddlers but only on older children (6-11 years) which is not considered relevant for this project.			
DIBP (di-iso-butyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Bekö et al. 2013	Indoor air and dust (estimated) and total exposure (biomonitoring)	Measurement of phthalates in dust (see above) Exp. indoor calculated from dust levels Children 3-6 years (internal dose): Median: 1.95 µg/kg/d 95-perc.: 7.97 µg/kg/d Max: 133.2 µg/kg/d Other exposure (food + articles): Children 3-6 years (internal dose): Median: 1.24 µg/kg/d 95-perc.: 8.09 µg/kg/d Max: 146 µg/kg/d	Data for 3-6 years old children considered realistic for **toddlers** as well. Indoor dust/air Other exposure, food, articles etc. **Sum, Danish data biomonitoring**	1.95 µg/kg/d (int) 1.24 µg/kg/d (int) **3.19 µg/kg/d** (int)	7.97 µg/kg/d (int) 8.09 µg/kg/d (int) **16.06 µg/kg/d** (int)
ECHA 2016	Various articles Indoor env. Food	**Infants** (6-12 months) Articles: Median: 1.06 µg/kg/d Worst case: 8.16 µg/kg/d Indoor env.: Median: 0.27 µg/kg/d Worst case: 1.41 µg/kg/d Food: Median: 1.03 Worst case: 9.02 µg/kg/d	Articles Indoor env. Food **Sum EU data**	**1.06 µg/kg/d (int)** **0.27 µg/kg/d (int)** **1.03 µg/kg/d (int)-** **2.37 µg/kg/d (int)**	**8.16 µg/kg/d (int)** **1.41 µg/kg/d (int)** **9.02 µg/kg/d (int)** **18.59 µg/kg/d (int)**

		No data on toddlers but only on older children (6-11 years) which is not considered relevant for this project.			
BBP (butyl-benzyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Bekö et al. 2013	Indoor air and dust (estimated) and total exposure (biomonitoring)	Measurement of phthalates in dust (see above) Expousre indoor calculated based on levels in dust: Children 3-6 years (internal dose): Median: 0.030 µg/kg/d 95-perc.: 0.16 µg/kg/d Max: 0.54 µg/kg/d	Data for 3-6 years old children considered realistic **for toddlers** as well. Indoor dust/air	0.030 µg/kg/d (int)	0.16 µg/kg/d (int)
		Other exposure (food + articles): Children 3-6 years (internal dose): Median: 0.46 µg/kg/d 95-perc.: 2.74 µg/kg/d Max: 22.2 µg/kg/d	Other exposure, food, articles etc.	0.46 µg/kg/d (int)	2.74 µg/kg/d (int)
			Sum Danish data, biomonitoring	**0.49 µg/kg/d (**int)	**2.90 µg/kg/d** (int)
ECHA 2016	Various articles Indoor env. Food	**Infant**s (6-12 months) Articles: Median: 0.31 µg/kg/d Wirst case: 2.43 µg/kg/d	Articles	**0.31 µg/kg/d (int)**	**2.43 µg/kg/d (int)**
		Indoor env.: Median: 0.08 µg/kg/d Worst case: 0.42 µg/kg/d	Indoor env.	**0.08 µg/kg/d (int)**	**0.42 µg/kg/d (int)**
		Toddlers, food: Median: 0.0 µg/kg/d Worst case 0.0.3 µg/kg/d	Food	**0.0 µg/kg/d**	**0.0 µg/kg/d**
			Sum EU data	**0.39 µg/kg/d (int)**	**2.85 µg/kg/d (int)**

		No data on toddlers but only on older children (6-11 years) which is not considered relevant for this project.			
DINP (di-iso-nonyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Fromme et al. 2013	Biomonitoring, Germany	**Toddlers** (15-21 months) Average intake Median: 0.9 µg/kg/d 95-perc: **2.3 µg/kg/d** High intake Median: 2.6 µg/kg/d 95-perc: **9.1 µg/kg/d**		**2.3 µg/kg/d (int)**	**9.1 µg/kg/d (int)**
Dipentyl phthalatee					
No data found					
Di-n-hexyl phthalate					
No data found					
DnOP (Di-n-octyl phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Fromme et al. 2013 Sioen et al 2012	Food Food	Estimated dietary exposure from data on content in food and food consumption of German children Toddlers (15-21 months) Average intake Median: 0.01 µg/kg/d 95-perc: 0.04 µg/kg/d High intake Median: 0.02 µg/kg/d 95-perc: 0.35 µg/kg/d Estimated intake based in content in food and intake of food in Belgium Children 2.5-6.5 years Average intake	Data on toddlers preferred compared to data on older children (2.5 – 6.5 years).	**0.04 µg/kg/d (int)**	**0.35 µg/kg/d (int)**

		Median: 0.033 µg/kg/d 95-perc: 0.050 µg/kg/d High intake Median: 0.150 µg/kg/d 95-perc: 0.256 µg/kg/d		0.050 µg/kg/d	0.256 µg/kg/d
Di-cyclo-hexyl-phthalate (DCHP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Sioen et al 2012	Food	Estimated intake based in content in food and intake of food in Belgium Children 2.5-6.5 years Average intake Median: 0.056 µg/kg/d 95-perc: 0.106 **µg/kg/d** High intake Median: 0.236 µg/kg/d 95-perc: 0.383 **µg/kg/d**	Data used as intake estimates for toddlers (due to lack of such data)	**0.106 µg/kg/d (int)**	**0.383 µg/kg/d (int)**
di-2-propylheptyl phthalate (DPHP)					
Fromme et al. 2013	Food	Estimated dietary exposure from data on content in food and food consumption of German children Toddlers (15-21 months) Average intake Median: 0.06 µg/kg/d 95-perc: 0.10 µg/kg/d High intake Median: 0.236 µg/kg/d 95-perc: 0.26 µg/kg/d		**0.10 µg/kg/d (int)**	**0.26 µg/kg/d (int)**
BfR 2011	Toys (plastic duck)	48% DPHP content Child (½-1 year), Estimated exposure, worst case: 135 µg/kg/d	**Specific toy scenario**		**135 µg/kg/d (int)**
Comments For DEHP, DBP, DiBP, BBP, the exposure estimates chosen for further risk assessment are based on Danish biomonitoring data (Bekö et al. 2014) and the exposure estimates in relation to 3-6 years old children. No such data on toddlers is available, however, it is considered possible also to use these data on toddlers. ECHA (2016) provides updated exposure estimates for infants					

based on exposure modelling (no data on toddlers). DiNP estimates are based on biomonitoring data on 12-21 months old toddlers (Froalslmme et al. 2013). DnOP,DCHP, and DPHP exposure estimates are based on German (Fromme et al. 2013) and Belgian (Sioen et al. 2012) data on food content and food consumption of children. It was not possible due to lack of data to provide exposure estimates for dipentylphthalate and di-n-hexylphthalate

Human biomonitoring: The urinary phthalate concentrations have been measured several Danish studies of Danish children adult women/pregnant women. Exposure calculations have been performed for both children and mothers (Bekö 2013; Frederiksen 2013; Fromme 2013). Exposure calculations by Bekö (2013) and Fromme (2013) are specified above and taken forward in the evalutation. The calculated exposure estimations for children aged 6-11 by Frederiksen are listed below:
DiBP: 2.75 µg/kg bw/d (7.55 µg/kg bw/d)
DnBP: 0.856 µg/kg bw/d (2.23 µg/kg bw/d)
BBzP : 0.227 µg/kg bw/d (1.1 µg/kg bw/d)
DEHP: 2.69 µg/kg bw/d (12.5 µg/kg bw/d)
DiNP**:** 1.2 µg/kg bw/d (11.3 µg/kg bw/d)
For the majority of the phthalates the exposure seems higher in children compared to adults, except for MEP, which is a phthalate often found in cosmetics. The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population
Furthermore, the exposure for infants fed with breastmilk was estimated based on measurements in human milk. Infant exposure from milk: MEHP (DEHP): Median: 5.158 µg/kg bw/d, max: 20.381 µg/kg bw/d, MnBP (DnBP), median: 1.079 µg/kg bw/d, max: 4.978 µg/kg bw/d and MiBP (DiBP) median: 3.508 µg/kg bw/d max: 9.999 µg/kg bw/d

References

Bekö G, Weschler CJ, Langer S, Callesen M, Toftum J, Clausen G. Children's phthalate intakes and resultant cumulative exposures estimated from urine compared with estimates from dust ingestion, inhalation and dermal absorption in their homes and daycare centers. PLoS One. 2013 Apr 23;8(4):e62442.
BfR 2011 German Federal Institute for Risk Assessment (BfR)
ECHA (2016). ANNEX XV RESTRICTION REPORT. PROPOSAL FOR A RESTRICTION SUBSTANCE NAMES: FOUR PHTHALATES (DEHP, BBP, DBP, DIBP).
Fromme H, Gruber L, Schuster R, Schlummer M, Kiranoglu M, Bolte G, Völkel W. Phthalate and di-(2-ethylhexyl) adipate (DEHA) intake by German infants based on the results of a duplicate diet study and biomonitoring data (INES 2). Food Chem Toxicol. 2013 Mar;53:272-80.
Sioen et al. (2012) Phthalates dietary exposure and food sources for Belgian preschool children and adults. Environ Int. Nov 1;48:102-8.

UV-filters

Benzophenone 3 (BP-3)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012 Danish EPA 2015 Danish EPA 2009	Cosmetics	Up to 6% in sunscreen. Typical and worst case scenario for children is 50% of adult dose i.e. 9 g/d and 2 x 9 g/d. (Danish EPA 2009) Typical scenario: 9 g/d x 60mg/g / 13 kg = 42 mg/kg/d Worst case: 2 x 9 g/d x 60 mg/g / 13 kg = 83 mg/kg/d Specific absorption rate of 4% (Danish EPA 2012). Default value of 10% used in Danish EPA (2015).	Danish EPA (2009) made expousre calculations using a maximum content of 10% in sunscreen and a dermal absorption facto of 4%. These calculations have been modified for the purpose of this project using the recent adopted maximum limit of 6% in cosmetics.	**42 mg/kg/d (d)** **1.7 mg/kg/d (int)**	**83 mg/kg/d (d)** **3.35 mg/kg/d (int)**
2-ethylhexyl 4-methoxycinnamate (OMC)					
Danish EPA 2012 Danish EPA 2015 Danish EPA 2009	Cosmetics	Up to 10% in sunscreen. Typical and worst case scenario for children is 50% of adult dose i.e. 9 g/d and 2 x 9 g/d. (Danish EPA 2009) Typical scenario: 9 g/d x 100 mg/g / 13 kg = 69 mg/kg/d Worst case: 2 x 9 g/d x 100 mg/g / 13 kg = 138 mg/kg/d Specific absorption rate of 2 **%** (Danish EPA 2012). Default value of 10% used in Danish EPA (2015).		**69 mg/kg/d (d)** **1.4 mg/kg/d (int)**	**138 mg/kg/d (d)** **2.8 mg/kg/d (int)**
Comments:					
Human biomonitoring: Human biomonitoring of the UV-filter BP-3 have been performed in two Danish studies of Danish children adult women and document wide exposure to this particular filter. Exposure calculations were performed for children 6-10 years of age (mean: 26.7 ng/kg bw/d, 1388 ng/kg bw/d 95p). The calculated mean exposure of BP-3 is lower compared to values estimated by the Danish EPA, where the worst case estimates are more similar.					

References:
Danish EPA (2009). 2-åriges udsættelse for kemiske stoffer. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 103, 2009.
Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Survey of chemical substances in consumer products no. 117. Danish EPA.

Danish EPA (2015). Survey and health assessment of UV filters. Survey of chemical substances in consumer products no. 142. Danish EPA.

Other substances

Acrylamide					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2015	Food	Median: Infants: 0.8-1.0 µg/kg/d Toddlers: 1.3-1.4 µg/kg/d 95-percentiles: Infant: 1.8-2.1 µg/kg/d Toddlers: 2.3-2.4 µg/kg/d	Exposure for toddlers selected (highest exposure)	1.4 µg/kg/d (o)	2.4 µg/kg/d (o)
MEFD 2016	Drinking water	Limit value: 0.1 µg/L	0.03 L/kg/d water ingestion of toddlers (mean) 0.08 L/kg/d water ingestion of toddlers (95-perc)	0.003 µg/kg/d (o)	0.008 µg/kg/d (o)
Aggregated exposure taken forward in evaluation:				**1.4 µg/kg/d (o)**	**2.4 µg/kg/d (o)**
Comments: The exposure estimates are considered as reliable. No other relevant sources for exposure could be found. Contribution from drinking water contribution is considered insignificant.					
Human biomonitoring: In a biomonitoring study from Germany (Heudorf et al., 2009) the level of exposure in 5-6 year old German children based on urinary measurements of acrylamide metabolites were estimated, and found levels (mean: 0.54 µg/kg bw/d.; 95-perc: 1.91 µg/kg bw/d) somewhat lower compared to the estimations given by EFSA (2015)					

References

EFSA (2015). EFSA opinion on acrylamide in food. EFSA Journal 2015;13(6):4104.
Heudorf et al (2009) Acrylamide in children – exposure assessment via urinary acrylamide metabolites as biomarkers. Int. J. Hyg. Environ. Health 212: 135–141
MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Siloxane D4					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
MST 2012a	Cosmetics Sunscreen	No estimations were calculated for children			
SCCS 2010	Cosmetics Sunscreen	No estimations were calculated for children			
Pieri 2013	Indoor air	Average daily intake based on the sum of 6 siloxane in samples from different indoor environments in UK		No specific calculations were made for D4.	No specific calculations were made for D4.

		and Italy. UK children: 3188 µg/d Italy children: 1261 µg/d No specific calculations were made for D4.			
Comments: There are no specific estimations of the exposure to D4 in children. The study from Italy (by Pieri) did calculate exposure estimates, however, the estimates was based on a total of 8 siloxanes and therefore no specific estimates are available for D4. The study does reveal, that exposure from indoor air may be an important contributor to the total siloxane exposure. However, as no specific exposure estimations exists for D4 in children, this compound is not taken further for risk assessment.					
Human biomonitoring: No human biomonitoring study within the identified criteria were found					

References:

MST 2012a: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende

SCCS 2010: Scientific Committee on Consumer Safety OPINION ON Cyclomethicone. SCCS/1241/10

Pieri F, Katsoyiannis A, Martellini T, Hughes D, Jones KC, Cincinelli A. Occurrence of linear and cyclic volatile methyl siloxanes in indoor air samples (UK and Italy) and their isotopic characterization. Environ Int. 2013 Sep;59:363-71.

Triclosan

Selected References	Source of exposure	Exposure	Further calculations/ modifications	Mean exposure (oral, dermal, inhal, intern)	Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)
Danish EPA 2012	Cosmetics Dust	Only data on adults: Pregnant women: Dust (µg/kg bw/day): Mean: 0.0015, high 0.0002 Cosmetics (toothpaste / deodorant at max concentration of 0.3%) Only toothpaste: 7.3 µg/kg/day Both (high exp.): 22 µg/kg/day	Toothpaste exposure scenario not considered relevant for toddlers, as triclosan has only been found in one specific toothpaste (for adults) in DK.	-	-
Geens et al. 2009	Dust	Toddlers Average dust intake: 11-87 µg/d (0.95 - 7.7 µg kg/d) High dust intake: 44 - 347 µg/d (3.8 - 30 µg kg/d)		**7.7 µg kg/d (o)**	**30 µg kg/d (o)**
Comments: A Danish survey from 2006 indicated that only very few cosmetic products contained triclosan. In the survey only one toothpaste with triclosan was found. Infant exposure to triclosan from breast milk has been shown to be significantly lower than triclosan exposure of the mother, based on a comparison of triclosan concentrations in breast milk					

and plasma (SCCS 2009).
Human biomonitoring: The urinary triclosan concentrations have been measured several Danish studies of Danish children adult women/pregnant women. The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population. Exposure calculations have not been performed on measurements from the Danish population or on children in similar countries, however, a study from Belgium (Geens 2015) estimated the exposure in obese adults to be 490 ng/kg bw d (90-perc: 565 ng/kg bw/d), which is lower compared to the estimates from the Danish EPA.

References:

Danish EPA (2012). http://www.mst.dk/service/publikationer/publikationsarkiv/2012/apr/exposure-of-pregnant-consumers-to-suspected-endocrine-disruptors/. Kortlægning af kemiske stoffer i forbrugerprojekter nr. 117. Miljøstyrelsen.

Geens et al. (2009). Assessment of human exposure to Bisphenol-A, Triclosan and Tetrabromobisphenol-A through indoor dust intake in Belgium. Chemosphere Volume 76, Issue 6, August 2009, Pages 755–760

Geens et al. (2015). Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals. Environ Int. 2015 Mar;76:98-105.

SCCP (2009) Scientific Committee on Consumer Products, Opinion on triclosan, SCCP/1192/08

Appendix 6b

Exposure estimates for pregnant women/ unborn children

The tables below contain ***six columns***:

Selected references: indicating the literature found most relevant for exposure estimations (i.e. the references identified in appendix 3 with a scoring of ++ or +++ and further literature identified during the process for this more detailed exposure assessment).

Source of exposure: describe the specific exposure source(s).

Exposure: indicate the values of the exposure estimates given in the reference.

Further calculations/ modifications: explains when further specific calculations or modifications of the data are necessary for the purpose of generation of exposure estimates for this project.

Mean exposure: in this column the *typical or mean/average exposure estimate* is given and the relevant exposure route is indicated. (Intern) is indicated if the internal dose (i.e. the systemic absorbed dose is indicated from the reference).

Worst-case/95 percent exposure: in this column, a *realistic worst case* or *95-percentile exposure estimate* is given and the relevant exposure route is indicated. (Intern) is indicated if the internal dose (i.e. the systemic absorbed dose is indicated from the reference).

Furthermore the tables contain a **Comment box** in which the further information, explanation or conclusions for the purpose of this project is given. Also, the tables contain a box for the indication and short discussion of available **human biomonitoring** (data from appendix 5c covering a table with the identified biomonitoring data).

Exposure estimates given in **bold** are the values that are considered most relevant for this project and the further risk assessment (i.e. these figures cover specifically the target groups of this projects (children below 3 years or unborn children/pregnant women), they are the most updated figures or the figures are considered most relevant for Danish conditions today).

NB: When specific calculations of background exposure of pregnant women in relation to chemical content in drinking water have been made the following exposure parameters are used (from NCM (2011)):
Mean and 95-percentile drinking water ingestion of 0.014 L/kg/d and 0.043L/kg/d.

Antioxidants

BHA					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012a	Food As food additive	Adults Mean: 0.03-0.12 mg/kg bw/d High level (95-perc): 0.08-1.12 mg/kg bw/d		**0.12 mg/kg bw/d (o)**	**1.12 mg/kg bw/d (o)**
	Food contact materials	Estimated for adults: 0.43 mg/kg bw/d		(0.43 mg/kg bw/d (o))*	-
	Cosmetics	**No data available**			
MEFD 2016	Drinking water	**Limit value:** 0.5 µg/l	0.014 L/kg/d water ingestion of pregnant women (mean) 0.043 L/kg/d water ingestion of pregnant women (95-perc)	**0.007 µg/kg bw/d (o)**	**0.0215 µg/kg bw/d (o)**
This project	Cosmetics	Separate exposure estimations will be made in chapter 6 based on analytical data made during this project.			
	Vitamin pills	Data from Danish manufacturers/ importers of vitamin pills indicate that the use of the substance recently has been phased out (Danish EPA communication 2016). Thus, exposure from vitamin pills is not considered relevant.			
Aggregated exposure taken forward in evaluation (Food additive + contact materials+ drinking water):				**0.13 mg/kg bw/d (o)**	**1.14 mg/kg bw/d (o)**
Comments: The estimates on BHA exposure are lacking data from food contact materials. EFSA based their exposure estimates from food contact materials on the assumption that individuals consume 1 kg of food packed in plastics regardless of their age. *However, preliminary Danish data indicate no migration of BHA so exposure from FCM will not be considered further (Personal communication from the Danish Environmental and Food Agency 2016). Further, the potential contribution from cosmetics or pharmaceutical will be considered separately cannot be estimated due to lacking of data on the use in these products. BHA was not found in the Danish database on consumer products.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References
EFSA Journal 2012;10(7):2759. SCIENTIFIC OPINION Statement on the safety assessment of the exposure to butylated hydroxyanisole E 320 (BHA) by applying a new exposure assessment methodology.
EFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg

BHT					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2012b	Food As food additive Food contact materials Cosmetics	Adults Mean: 0.01-0.03 mg/kg bw/d High level (95-perc): 0.03-0.17 mg/kg bw/d Estimated for adults: 0.05 mg/kg bw/d		**0.03 mg/kg bw/d (o)** (0.05 mg/kg bw/d (o))*	**0.17 mg/kg bw/d (o)**
Data Danish EPA database on consumer products	Consumer products for children including gel nails, mobile phones, computers etc.	BHT was detected in the products but the exposure was not estimated			
Lundebye et al. 2010	Farmed fish	Adult: 0.037 mg/kg bw/d From ingestion of 300 g farmed salmon			**0.037 mg/kg bw/d (o)**
This project	Cosmetics Vitamin pills	Separate exposure estimations, see chapter 6.6.1. Body lotion: 480 µg/kg bw/d (dermal), corresponding to 19.2 µg/kg bw/d (internal dose). Sunscreen and body lotion total: 2016 µg/kg bw/d (dermal),		300 µg/kg bw/d (dermal), corresponding to 12 µg/kg bw/d (internal dose)	1260 µg/kg bw/d (dermal), corresponding to 50.4 µg/kg bw/d (internal dose)

		corresponding to 80.6 µg/kg bw/d (internal dose). Data from Danish manufacturers/ importers of vitamin pills indicate that the use of the substance recently has been phased out (Danish EPA communication 2016). Thus, exposure from vitamin pills is not considered relevant.			
Aggregated exposure taken forward in evaluation (Food additive + contact materials + farmed fish):				**0.03 mg/kg bw/d ((o))**	**0.21 mg/kg bw/d ((o))**
Comments: The estimates on BHT exposure are lacking data from food contact materials. EFSA based their exposure estimates from food contact materials on the assumption that individuals consume 1 kg of food packed in plastics regardless of their age. *However, preliminary Danish data indicate no migration of BHT so exposure from FCM will not be considered further (Personal communication from the Danish Environmental and Food Agency 2016). . BHT was measured in several consumer products relevant for adult women and a contribution from these products must also be expected, however the level of exposure estimated from these sources was not determined. Further the potential contribution from cosmetics or pharmaceutical cannot be estimated due to lacking of data on the use in these products.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

EFSA 2012: Scientific Opinion on the re-evaluation of butylated hydroxytoluene BHT (E 321) as a food additive. EFSA Journal 2012;10(3):2588

Lundebye et al. 2010. Levels of synthetic antioxidants (ethoxyquin, butylated hydroxytoluene and butylated hydroxyanisole) in fish feed and commercially farmed fish. Food Additives & Contaminants: Part A, 27:12, 1652-1657

Brominated compounds

HBCDD					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish DTU 2015	Food	**Adults** Adults, average: 0.19 ng/kg/d Adults, 95-perc: 0.75 ng/kg/d	The Danish exposure estimates indicate exposure in the lower range of the EU-range	**0.0002 µg/kg/d (o)**	**0.0008 µg/kg/d (o)**
EFSA 2011a		**Adults** Adults, average: 0.09 - 0.99 ng/kg/d Adults, 95-perc: 0.39 – 2.07 ng/kg/d			
TBBPA					
EFSA 2011b	Food	**Adults.** Worst case from high level consumption of fish: 2.6 ng/kg/d (however data on other food item is missing)			**0.0026 µg/kg/d (o)**
	Indoor air	Mean TBBPA concentration in homes offices and public microenvironments ranged from 16 to 93 pg/m3.	Inhalation of 20m^3/d of a 60 kg women = 5.3 and 31 pg/kg/d or 0.000005 to 0.000031 µg /kg/d i.e. insignificant exposures		
Danish EPA 2012	Indoor air	Indoor air levels of average and maximum levels of 1.04 and 14.6 µg/m^3 resulting in exposure of 0.26 and 3.65 µg /kg/d (However, the measured levels are in relation to the working environment).			
Deca-BDE (BDE-209)					
EFSA 2011c	Food	**Adults** Adults, average: 0.003 µg/kg/d Adults, high: 0.005 µg/kg/d		**0.003 µg/kg/d (o)**	**0.005 µg/kg/d (o)**
Tetra + Penta-DBE (BDE-47 + BDE-99)					
EFSA 2011c	Food	**Adults (BDE-47 + BDE-99)** Adults av.: 0.002 + 0.0007 µg/kg/d Adults high : 0.007 + 0.0014 µg/kg/d	BDE-47 BDE-99	**0.002 µg/kg/d (o)** **0.0007 µg/kg/d (o)**	**0.007 µg/kg/d (o)** **0.0014 µg/kg/d (o)**

Hexa-BDE (BDE-153)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2011c	Food	**Adults** Adults, average: 0.00042 µg/kg/d Adults, high: 0.00089 µg/kg/d		**0.00042 µg/kg/d**	**0.00089 µg/kg/d**
Comments. For all the brominated flame retardants food is the primary source for the population exposure. Exposure from other sources are considered minor/ insignificant. Adult women may however, as indicated by Danish EPA 2012 by subjected to significant exposure through inhalation at specific work places working with electronic equipment.					
Human biomonitoring: The levels of poly brominated flame retardants have been measured several times in Danish children and women. Exposure calculations have not been made for adults, but widespread exposure to PBDEs is documented. Exposure calculations have been made for infants based on breast milk consumption. See appendix 5c.					

References.

Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Kortlægning af kemiske stoffer i forbrugerprojekter nr. 117. Miljøstyrelsen.

Danish EPA (2014). Survey of brominated flame retardants. Part of the LOUS-review. Environmental Project No. 1536. Danish Environmental Protection Agency.

DTU (2015). Chemical contaminants. Food monitoring 2004-2011. National Food Institute. Technical University of Denmark. Division of Food Chemistry

EFSA (2011a). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Hexabromocyclododecanes (HBCDDs) in Food. EFSA Journal 2011;9(7):2296. [118 pp.] doi:10.2903/j.efsa.2011.2296. Available online: www.efsa.europa.eu/efsajournal

EFSA (2011b). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Tetrabromobisphenol A (TBBPA) and its derivatives in food. EFSA Journal 2011;9(12):2477. [67 pp.] doi:10.2903/j.efsa.2011.2477. Available online: www.efsa.europa.eu/efsajournal

EFSA (2011c). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Journal 2011;9(5):2156. [274 pp.] doi:10.2903/j.efsa.2011.2156. Available online: www.efsa.europa.eu/efsajournal

Chlorinated compounds

PCB/TCDD					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
PCBtotal. Sum of 6 PCB indicators as reference for other congeners (PCB6): PCB-28,-52,-101,-138,-153,-180.					
EFSA 2012	Food	Adult (EU): Mean: 3.8-11.5 ng/kg/d 95-perc: 8.1-33 ng/kg/d Adult (DK): Mean: 5.4-6.3 ng/kg/d 95-perc: 10.8-11.8 ng/kg/d		**6.3 ng PCB6/kg/d (o)**	**11.8 ng PCB6/kg/d (o)**
Danish HMA 2013	Evaporation to indoor air from building materials	Limit values for total PCBs: 300-3 000 ng /m3 corresponding to 60-600 ng PCB6/m^3	Adult: inhalation of 20 m^3/d 1200-12000 ng PCB6 (NDL)/m^3 (bodyweight 60 kg)	20 ng PCB6/kg/d (inh)	**200 ng PCB6/kg/d (inh)**
	Aggregate typical exposure, mean (no indoor contribution) **Aggregate worst case exposure including high indoor exposure**			**6.3 ng PCB6/kg/d (o)**	**11.8 ng PCB6/kg/d (o) +** **200 ng PCB6/kg/d (inh)**
DL-PCBs + dioxins					
EFSA 2012	Food	Adult (EU): Mean: 0.57-1.64 pg TCDD eqv/kg/d 95-perc: 1.9-4.5 pg TCDD eqv/kg/d Adult (DK): Mean: 1.06 pg TCDD eqv/kg/d 95-perc: 2.3 pg TCDD eqv/kg/d		**1.06 pg TCDD eqv/kg/d (o)**	**2.3 pg TCDD eqv/kg/d (o)**
Comments: The EFSA data is considered the best data for exposure estimation as estimation of exposure of the Danish population is based on monitoring results from 2008-2010. The estimates given by DTU Food 2015 is based on data from 2004-2011, i.e. older data may affect the exposure estimations. For both non-dioxin like PCBs and dioxin-like PCBs and dioxins in general the primary exposure is from ingestion of food. For non-dioxin like PCBs a significant additional exposure that exceeds exposure from food may come from inhalation of indoor air contaminated with PCBs evaporated (dominated by the low molecular PCB congeners) from PCB-containing building materials (typically sealings).					
Human biomonitoring: The plasma concentrations of PCBs have been measured in Danish children and adults. Measurements have also been made on residents of known PCB contaminated buildings. Exposure calculations have been performed for infants (see table for children < 3 years) based on the PCB concentrations measured in breast milk (Schlumpf 2010). The measurements show that the Danish population is still exposed to PCBs even though their use have been banned for many years. Further, the study of inhabitants of contaminated buildings show that indoor air may be an important source to PCB exposure, if living in buildings built with PCB-containing material.					

References

Danish HMA (2013). HEALTH RISKS OF PCB IN THE INDOOR CLIMATE IN DENMARK – background for setting recommended action levels. Background report prepared for Danish Health and Medicines Authority by Nordic Institute of Sustainable Products and Environmental Chemistry and Toxicology

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. Edition, June 2015

EFSA (2012). SCIENTIFIC REPORT OF EFSA. Update of the monitoring of levels of dioxins and PCBs in food and feed. European Food Safety Authority. EFSA Journal 2012;10(7):2832.

Tetrachloroethylene					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Indoor air; Indoor air + dry cleaned clothes	< 3 µg/m^3 in homes without known tetrachloroethylene sources 92 µg/m^3 as average level during 14 days after parents bringing tetrachloroethylene dry cleaned clothes home (small un-vented flat).		**3 µg/m^3 (inh)**	92 µg/m^3 (inh)
MEFD 2015	Indoor air	100 µg/m^3 as regulatory limit value for migration of tetrachloroethylene from a dry cleaning store to flats in the same building.			**100 µg/m^3 (inh)**
Danish EPA 2014	Wearing dry cleaned clothes	Wearing freshly dry cleaned clothes. Total exposure (inh+ dermal): 46 mg/d	767 µg/kg/d for a pregnant women with a body weight of 60 kg		**767 µg/kg/d (inh + d)**
Comments: Exposures in relation to dry cleaning of clothes are considered the only significant exposures for consumers and the general population.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References:

Danish EPA (2014). Evaluation of health hazards by exposure to Tetrachloroethylene and proposal of a health-based quality criterion for ambient air Environmental Project No. 1563.

Danish EPA (2016).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

MFED (2015). Bekendtgørelse nr 1457 af 07/12/2015 Bekendtgørelse om etablering og drift af renserier (Statutory order regarding the establishment and operation of dry cleanings stores). Ministry for Environment and Food of Denmark.

Trichloroethylphosphate(TCEP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
ARCADIS 2011/ EU-RAR 2009	Combined exposures from dermal contact to furniture and dust and inhalation exposure	Adult, reasonable worst case: Total exposure 4.5 µg/kg bw/d (internal)		-	**4.5 µg/kg bw/d (combined internal exposure)**
Comments: This exposure estimate is considered uncertain and only applies to one specific scenario. The probability for exposure today has been reduced as the use of TCEP in Europe is subjected to authorization under REACH.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

ARCADIS (2011). Contract number 17.020200/09/549040. Identification and evaluation of data on flame retardants in consumer products P3-402

EU-RAR (2009). European Union Risk Assessment Report on TRIS (2-CHLOROETHYL) PHOSPHATE, TCEP, July 2009, p 1-213

Fluorinated compounds

PFAS					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
PFOA					
Livsmedelsverket 2013	Food	Adults Average: 0.57 ng/kg/d 95-perc.: 0.86 ng/kg/d	Based on Swedish data	**0.57 ng/kg/d (o) (average)**	**0.86 ng/kg/d (o) (95-perct)**
EFSA	Food	Adults Average: 0.13 – 3.2 ng/kg/d 95-perc.: 0.28 – 5.4 ng/kg/d	Based from data from EU countries		
Haug et al. 2011	Dust	Ingestion of 50 mg dust/d: 0.012 ng/kg/d Ingestion of 200 mg dust/d: 0.049 ng/kg/d	Norwegian data on dust content	**0.012 ng/kg/d (o)**	**0.049 ng/kg/d (o)**
	Air	Medium, air: 0.010 ng/kg/d High scenario: 0.035 ng/kg/d	Norwegian data on air content	**0.010 ng/kg/d (inh)**	**0.035 ng/kg/d (inh)**
ECHA/RAC 2015	Total exposure	Adults Median scenario: 0.26 – 6.1 ng/kg/d High scenario: 4.1 – 44 ng/kg/	Worst case total exposure of more than 6.1 ng/kg/d seems unrealistic for Danish conditions		**6.1 ng/kg/d (o) (as specific worst case)**
	Aggregate exposure, food, dust, air			**0.59 ng/kg/d (o+inh)**	**0.94 ng/kg/d (o+inh)**
PFOS					
DTU Food 2015	Food	Adults Average: 0.45ng/kg/d	Based on Danish data	**0.45 ng/kg/d (o) (average)**	
Livsmedelsverket 2013	Food	Adults Average: 0.37 ng/kg/d 95-perc.: 1.15 ng/kg/d	Based on Swedish data		**1.15 ng/kg/d (o) (95-perc)**
Haug et al. 2011	Dust	Ingestion of 50 mg dust/d: 0.003 ng/kg/d Ingestion of 200 mg dust/d: 0.011 ng/kg/d	Norwegian data on dust content	**0.003 ng/kg/d (o)**	**0.011 ng/kg/d (o)**
	Air	Medium, air: 0.015 ng/kg/d High scenario: 0.077 ng/kg/d	Norwegian data on air content	**0.015 ng/kg/d (inh)**	**0.077 ng/kg/d (inh)**

EFSA	Food	Adults Average: 0.8 – 3.0 ng/kg/d 95-perc.: 3.1 – 6.8 ng/kg/d	Based from data from EU countries		**6.8 ng/kg/d (o)** **(as specific worst case)**
	Aggregate exposure, food+dust+air			**0.47 ng/kg/d (o+inh)**	**1.24 ng/kg/d (o+inh)**
PFHxS					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Livsmedelsverket 2013	Food	Adults Average: 0.03 ng/kg/d 95-perc.: 0.05 ng/kg/d	Based on Swedish data	**0.03 ng/kg/d (o)**	**0.05 ng/kg/d (o)**
EFSA	Food	Adults Average cons, average: 0.03 – 1.22 ng/kg/d High consumers, average: 0.13 – 2.25 ng/kg/d	Based from data from EU countries		
Comments: Preference is given to data from the Nordic countries. Worst case scenario is, however, based on estimates from EFSA and ECHA/RAC based on data from all EU countries. For the worst cases scenarios the content of PFOS and PFOA in air and dust found in the study by Haug et al. 2011 may contribute to about 7% and 10% compared to the 95-percentile dietary exposure.					
Human biomonitoring: The plasma concentrations of PFASs have been measured in several Danish studies of both pregnant women, non-pregnant women and children. Exposure calculations have not been performed from the serum/plasma levels, but the PFAS was detected in nearly all samples indicating widespread exposure. The biomonitoring studies show that women with more children have lower serum levels, which indicates that pregnancy and likely also breastfeeding status affects the PFAS levels in the blood.					

References

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. edition, juni 2015

ECHA/RAC (2015). Committee for Risk Assessment (RAC) Committee for Socio-economic Analysis (SEAC) Background document.to the Opinion on the Annex XV dossier proposing restrictions on Perfluorooctanoic acid (PFOA), PFOA salts and PFOA-related substances. ECHA/RAC/RES-O-0000006229-70-02/F. ECHA/SEAC/[reference code to be added after the adoption of the SEAC opinion]. 11September 2015.

EFSA (2012). SCIENTIFIC REPORT OF EFSA. Perfluoroalkylated substances in food: occurrence and dietary exposure. European Food Safety Authority. EFSA Journal 2012;10(6):2743

Haug et al. (2011).Characterisation of human exposure pathways to perfluorinated compounds--comparing exposure estimates with biomarkers of exposure. Environ Int. 2011 May; 37(4):687-93.

Livsmedelsverket (2013). Riskvärdering av perfluorerande alkylsyror i livsmedel och dricksvatten. Rapport 11-2013.

Hydrocarbons

Toluene					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data on indoor + outdoor+ microenvironments Mean: 11.7 µg/m^3 95-perct: 55.3 µg/m^3	Used for 95-perc. "back-ground level"		**55.3 µg/m^3 (inh)**
	Indoor air	Average level 9.1 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	These Danish data used typical exposure levels	**9.1 µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	One children´s room subjected to evaporation from stored gasoline outside in a shed. 230 µg/m^3	Used as a specific worse-case scenario		**230 µg/m^3 (inh)**
Xylenes					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data on indoor + outdoor+ microenvironments): Mean: 6.7 µg/m^3 95-perct: 42.3 µg/m^3	Used for 95-perc. "back-ground level"		**42.3 µg/m^3 (inh)**
	Indoor air	Average level 7.5 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**7.5 µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	One children´s room subjected to evaporation from stored gasoline outside in shed. 146 µg/m^3	Specific worse-case scenario		**146 µg/m^3 (inh)**
Ethylbenzene					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data on indoor +	Used for 95-perc. "back-ground level"		**8.2 µg/m^3 (inh)**

		outdoor+ microenvironments): Mean: 1.8 µg/m^3 95-perct: 8.2 µg/m^3			
	Indoor air	Average level 3.2 µg/m^3 measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**3.2 µg/m^3 (inh)**	
	Indoor air due to storage of gasoline	One children´s room subjected to evaporation from stored gasoline outside in shed. 37 µg/m^3	Specific worse-case scenario		**37 µg/m^3 (inh)**
Total C6-C12, alifatic, alicyclic and aromatic hydrocarbons					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (Eu data on indoor + outdoor+ microenvironments): Mean: 79 µg/m^3 95-perct: 232 µg/m3	Used for 95-perc. "back-ground level"	**79 µg/m^3 (inh)**	**232 µg/m^3 (inh)**
	Indoor air due to storage of gasoline	One children´s room subjected to evaporation from stored gasoline outside in shed. 1500 µg/m^3 (measured as TVOC)	Specific worse-case scenario		**1500 µg/m^3 (inh)**
	Indoor air	Average level < 338 µg/m^3 (measured as TVOC) measured in 18 children´s room in DK (may also be used for other rooms)	Danish data used typical exposure level	**338 µg/m^3 (inh)**	
Danish EPA-LOUS 2014a	Indoor air during painting using alkyd paint	Average levels: 470 - 600 mg/m^3 Worst case: 6140 mg/m^3	Specific scenario for product use	600 mg/m^3 (inh)	**6140 mg/m^3 (inh)**
Styrene					
Danish EPA 2016	Air	Daily exposure levels measured with portable devices (EU data on indoor + outdoor+ microenvironments): Mean: 0 µg/m^3 95-perct: 2.5 µg/m3	" 11 µg/day / 60 kg = 0.18 µg/kg/d	0 mg/m^3	**2.5 µg/m^3 (inh)**

Danish EPA-LOUS 2014b	Food	Adult exposure via food (3 µg/day) and from chewing gum (8 µg/day)		**0.18 µg/kg/d (o) (dose is corresponding to exposure to 0.6 µg/m^3 in air).**	**No specific value (mean expsure used for aggregate exp)**
	Aggregate exposure: oral and inhalation				**2.5 µg/m^3 (inh) +0.18 µg/kg/d (o)**
Comments: Data from portable measuring devices are used as these figures typically indicate higher exposure compared to the estimated combined exposure from ambient air, indoor air and air inside cars. These data are pooled from measurements in 11 European cities and may most likely overestimate Danish conditions. Danish EPA (2016) examined evaporation from building materials, furniture, electronics and toys relevant for children and children´s rooms, however, only very low hydrocarbon levels were measured. Thus, laboratory measurements of these articles and also measurement of a children´s room mock-up clearly underestimated exposure in real life (performed in 19 homes).					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

Danish EPA 2016).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

Danish-LOUS (2014a). Survey of white spirit. Environmental Project No. 1546. Part of the LOUS-review. Danish Environmental Protection Agency.

Danish-LOUS (2014b). Survey of styrene. Environmental Project No. 1612. Part of the LOUS-review. Danish Environmental Protection Agency.

Medicine

Paracetamol					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish medicines agency	Medicine	Adults: Mean exposure scenario: 16.67 mg/kg bw/d Maximum exposure: 66.67 mg/kg bw/d	Recommended dose for adults: 1g 3-4 times a day, with a maximum dose of 4 g per day. Mean exposure 1g/day Max exposure 4g/day Adult: 60 kg	**16.67 mg/kg bw/d (o)**	**66.67 mg/kg bw/d (o)**
Comments: It is evident from the research paper listed in table 3.1 under paracetamol, that the intake of medication with paracetamol is quite common in pregnant women. The estimation of paracetamol exposure is based on the recommended intake of the paracetamol containing medication, panodil. When evaluating the risk of paracetamol exposure, it must be taken into consideration that the exposure is based on self-medication, and the exposure will occur in intervals. Furthermore the benefits of the medication must be taken into consideration.					
Human biomonitoring: The urinary excretion of paracetamol have been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that paracetamol could be detected in nearly all samples. The concentration of paracetamol in the urine was not always dependent on the intake of paracetamol medication and the authors suggests other sources of paracetamol e.g. from the metabolism of the chemical aniline which is present in the diet.					

References: *Product summary of Panodil (paracetamol medication) from Danish Medicines Agency. Retrieved on 04.07.2016*

Metallic compounds

Aluminium					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
NSCFS 2013 and SCCS 2014 (identical values)	Food	Mean exposure, food: Adult: 0.29 mg/kg bw/week 95-percentiles, food: Adult: 0.67 mg/kg bw/week Internal: (For calculation of internal exposure a gastrointestinal absorption rate of 0.1 % used).	Weekly exposure converted to daily exposure by a factor of 1/7.	41 µg/kg/d (o) (**0.041 µg/kg/d** as internal dose)	96 µg/kg/d (o) (as **0.096 µg/kg/d** internal dose)
	Cosmetics	Adult women (Use of lipstick/lip gloss + antiperspirant): Mean use: 31.7 µg/kg/w as internal dose High use: 600 µg/kg/w as internal dose	Weekly exposure converted to daily exposure by a factor of 1/7.	External doses not given **4.5 µg/kg/d (int)**	External doses not given **85.7 µg/kg/d (int)**
MEFD 2016	Drinking water	Limit value: 200 µg/L	0,014 L/kg/d water ingestion, pregnant women (mean) 0.043 L/kg/d water ingestion, pregnant women (95-perc)	2.8 µg/kg/d (o) 0.003 µg/kg/d (int)	8.6 µg/kg/d (o) 0.009 µg/kg/d (int)
Comments: No other relevant exposure could be found. Systemic exposure from medical use in antacids (e.g. aluminiumaminoacetat or aluminium hydroxide) is not further considered as the intended use is for local treatment in the stomach and not for systemic treatment. Thus, the aluminium complexes used in the pharmaceutical preparations are selected for avoiding absorption and therefor a default absorption factor of 0.1% is not considered relevant for the medical use. Also, there may be exposure to aluminium from its use in vaccines, which may contain up to about 1 mg of aluminium (Oxford University 2016). Although some uncertainty applies to an oral absorption factor of 0.1% the exposure estimates as indicated for food, drinking water and cosmetics are considered valid for use in a risk assessment.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Oxford Universtity 2016.. http://vk.ovg.ox.ac.uk/vaccine-ingredients

NSCFS (2013). Risk assessment of the exposure to aluminium through food and the use of cosmetic products in the Norwegian population. Norwegian Scientific Committee for food safety. VKM- 05/04/2013

Lead					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
DTU Food 2015	Food	Total exposure (mean): Adults: 0.23 µg/kg/d Total exposure (95-perc): Adults: 0.41 µg/kg/d 99-perc (whole population > 4 years): 1,05 µg/kg/d		**0.23 µg/kg/d (o)**	**0.41 µg/kg/d (o)**
MST-LOUS 2014 MEFD 2016	Drinking water	Drinking water, average conc. of 0.9 µg/L: Pregnant women: 0.013 µg/kg/d Drinking water, high level at limit value of 10 µg/L: Pregnant women: 0.43 µg/kg/d		**0.013 µg/kg/d (o)**	**0.43 µg/kg/d (o)**
Aggregated exposure taken forward in evaluation (food, mean + drinking water concentration at 0.9 µg/L): **Aggregated exposure taken forward in evaluation (food worst case + drinking water concentration at 10 µg/L):**				**0.24 µg/kg/d (o)**	**0.84 µg/kg/d (o)**
Comments: The exposure estimates considered highly reliable, as they are based on Danish data on lead content in food. Relevant figures on lead exposure from other sources were not found. However, some exposure may apply to e.g. the wear of lead containing metallic jewelry (dermal/oral exposure) or from drinking from (old/ imported) crystal glass or enameled ceramic cups.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References

Danish EPA-LOUS (2014). Survey of lead and lead compounds. Environmental Project No. 1539. Part of the LOUS-review. Danish Environmental Protection Agency.
DTU Food 2015. Chemical contaminants. Food monitoring 2004-2011. National Food Institute. Technical University of Denmark. Division of Food Chemistry.
EFSA (2012) SCIENTIFIC REPORT OF EFSA. Lead dietary exposure in the European population. European Food Safety Authority. EFSA Journal 2012;10(7):2831
SCENIHR (2015). SCENIHR Opinion on The safety of dental amalgam and alternative dental restoration. Scientific Committee on Emerging and Newly Identified Health Risks. The SCENIHR adopted this opinion at the 10th plenary meeting on 29 April 2015.

Mercury					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Inorganic mercury					
DTU Food 2015	Food	**Inorganic mercury:** 4-74 years (mean): 0.012 µg/kg bw/d 4-74 years (95-perc): 0.034 µg/kg bw/d		0.012 µg Hg/kg/d (o)	0.034 µg Hg/kg/d (o)
MEFD 2016	Drinking water	**Inorganic mercury** At limit value of 1 µg/L		0.014 µg Hg/kg/d (o)	0.043 µg Hg/kg/d (o)
	Aggregated exposure food and drinking water at limit value			**0.026 Hg/kg/d (o)**	**0.077 Hg/kg/d (o)**
SCENIHR (2015)	Dental fillings	**Inorganic mercury:** Adults, range: 3-17 µg Hg/day (0.05-0.28 µg Hg/kg /d) Adult, average 10 µg Hg/day (0.17 µg Hg/kg /d)		**0.17 µg Hg/kg /d (o)**	**0.28 µg Hg/kg /d (o)**
Methylmercury:					
DTU Food 2015	Food	**Methylmercury:** 4-74 years (mean): 0.018 µg/kg bw/d 4-74 years (95-perc): 0.051 µg/kg bw/d		**0.018 µg Hg/kg/d (o)**	**0.051 µg Hg/kg/d (o)**
Comments: The exposure estimates are considered highly reliable as they are based on data of mercury content in food on the Danish market. Also, the adult population may be exposed to mercury from broken fluorescent light, as well as from old fever thermometers, barometers, etc. which may still be used, but are not sold anymore. The exposure from amalgam dental fillings clearly overweighs the exposure from other sources. Possible exposure to mercury from its use as preservative in vaccines (Thimerosal / ethyl-mercury) may be a further source of exposure. About 25µ Hg/dose (Netdoktor 2016).					
Human biomonitoring: The levels of mercury have been measured the hair of Danish children and their mothers. Exposure calculations have not been performed, but the intake of fish was significantly associated mercury concentrations in hair. The level of mercury in hair also increased with age in the women (Mørck 2015a).					

References

DTU Food (2015). Chemical contaminants 2004-2011. Food monitoring 2004-2011.3. Edition, June 2015

Mørck et al (2015a). The Danish contribution to the European DEMOCOPHES project: A description of cadmium, cotinine and mercury levels in Danish mother-child pairs and the perspectives of supplementary sampling and measurements. Environmental Research 141 (2015) 96–105

SCENIHR (2015). SCENIHR Opinion on The safety of dental amalgam and alternative dental restoration. Scientific Committee on Emerging and Newly Identified Health Risks. The SCENIHR adopted this opinion at the 10th plenary meeting on 29 April 2015.

Parabens

Propylparaben (PP) + Butylparaben (BP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Propylparaben (PP)					
SCCS 2013	Cosmetics	Women: 0.043 mg/kg bw/day (int)	Based on exposure to 17.4 g leave-on cosmetics with total concentration of 0.4% of PB + BB. The absorption rate was estimated to 3.7%. Used as worst case		0.043 mg/kg bw/day (int)
MST 2012	Cosmetics Sunscreen Air	Internal exposure doses: *Basic scenario (daily use of varipus cosmetics with a content of 0.1% (mean) and 0.4 % (maximum) PP, dermal abs of 3.7%)*) Mean: **2.72 µg/kg bw/d** Maximum: 19 µg/kg bw/d *Sunscreen:* *18 g/d (mean) and 36 g/d (maximum) sunscreen with a content of 0.1% (mean) and 0.4% (maximum) PP and dermal absorption of 3.7%:* Mean: 11.1 µg/kg bw/d Maximum: 88.8 µg/kg bw/d Indoor: Mean: 0.0003 µg/kg bw/d Maximum: 0.0009 µg/kg bw/d Total: Mean: 0.0003 µg/kg bw/d Maximum: 0.0009 µg/kg bw/d	For the purpose of this project the mean exposure estimates are used as a content of 0.4% of PP today is unrealistic, as the maximum limit today is set to 0.14% for PP + BP.	**Internal exposure doses:** **Basic scenario (cosmetics)** **2.72 µg/kg bw/d (int)** Indoor: 0.0003 µg/kg bw/d (int)	**Sunscreen:** **11.1 µg/kg bw/d (int)** Indoor: 0.0009 µg/kg bw/d (int)
Butylparaben (BP)					
SCCS 2013	Cosmetics	Women: 0.043 mg/kg bw/day (int)	Based on exposure to 17.4 g leave-on cosmetics with total concentration of 0.4% of PB + BB. The absorption rate was estimated to 3.7%.		0.043 mg/kg bw/day (int)

			Used as worst case		
MST 2012	Cosmetics Sunscreen	Internal exposure doses: *Basic scenario (daily use of varipus cosmetics with a content of 0.1% (mean) and 0.4 % (maximum) PP, dermal abs of 3.7%)*) Mean: **2.72 µg/kg bw/d** Maximum: 19 µg/kg bw/d *Sunscreen:* *18 g/d (mean) and 36 g/d (maximum) sunscreen with a content of 0.1% (mean) and 0.4% (maximum) PP and dermal absorption of 3.7%:* Mean: 11.1 µg/kg bw/d Maximum: 88.8 µg/kg bw/d Indoor: Mean: 0.0001 µg/kg bw/d Maximum: 0.0041 µg/kg bw/d	For the purpose of this project the mean exposure estimates are used as a content of 0.4% of PP today is unrealistic, as the maximum limit today is set to 0.14% for PP + BP.	Internal exposure doses: Basic scenario (cosmetics) 2.72 µg/kg bw/d (int) Indoor: 0.0001 µg/kg bw/d (int)	Sunscreen: 11.1 µg/kg bw/d (int) Indoor: 0.0041 µg/kg bw/d (int)
Comments: More detailed scenarios were given by the Danish EPA (2012) compared to SCCS (2013). The Danish scenarios cover an everyday scenario without sunscreen and a scenario specifically addressing sunscreen. . **Based on a max. conc. level of 0.14% instead of 0.1% a typically exposure to PP+ BB from the basic scenario of 3.8 µg/kg bw/d (int) can be calculated and a worst case scenario for using sunscreen of 16 µg/kg bw/d (int) can be calculated.**					
Human biomonitoring: Comments: The paraben concentrations of propyl- and butylparaben along with methyl- and ethylparabens, have been measured several Danish studies of Danish children adult women/pregnant women. Exposure calculations have been performed for infants based on levels measured in breast milk from Swiss mothers, but no exposure calculations were performed for adults. The measurements show that the detection of propyl- and butylparaben in the urine of Danish children and women are generally lower compared to the shorter chained parabens methyl- and ethylparaben. Further the measurements show that the highest exposure to parabens is among the youngest children and women.					

References:

SCCS 2013: Scientific Committee on Consumer Safety SCCS/1514/13. OPINION ON Parabens.

MST 2012: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer

Pesticides

Pesticides					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Jensen et al. 2015	Food	**Adults; men+ women** (µg/kg bw/day): Diazinon 0.0047 Pirimiphos-methyl 0.043 Dicofol (sum) 0.017 Procymidone 0.018 Dimethoate 0.0063 Carbaryl 0.043 Chlorfenvinphos 0.0028 Carbendazim and benomyl 0.087 Dithiocarbamates 0.21 Linuron 0.010 Methomyl and thiodicarb 0.0083 Methamidophos 0.0029 Imazalil 0.072 Oxydemeton-methyl (sum) 0.00074	It is in the publication indicated that women in average are exposed to a total amount of pesticides residues of 2.2 µg/kg bw/day compared to exposure of men and women combined of 1.9 µg/kg bw/day**. I.e. the figures should be corrected with a factor 2.2/1.9 = 1.16 for women for average consumption.** Further a group of high consuming women (fruit+ vegetables) were exposed to total residue exposure of 3.5 µg/kg bw/day, **i.e. a correction factor of 3.5/1.9 = 1.84 may be used for calculating high consumption exposure from the mean exposure value.**	**Women µg/kg bw/day (o)** **Diazinon 0.0055** **Pirimiphos-methyl 0.050** **Dicofol (sum) 0.020** **Procymidone 0.021** **Dimethoate 0.0073** **Carbaryl 0.050** **Chlorfenvinphos 0.0033** **Carbendazim and benomyl 0.101** **Dithiocarbamates 0.24** **Linuron 0.012** **Methomyl and thiodicarb 0.0096** **Methamidophos 0.0034** **Imazalil 0.084** **Oxydemeton-methyl (sum) 0.00086**	**Women µg/kg bw/day (o)** **Diazinon 0.0086** **Pirimiphos-methyl 0.079** **Dicofol (sum) 0.031** **Procymidone 0.033** **Dimethoate 0.012** **Carbaryl 0.079** **Chlorfenvinphos 0.0052** **Carbendazim and benomyl 0.16** **Dithiocarbamates 0.39** **Linuron 0.018** **Methomyl and thiodicarb 0.015** **Methamidophos 0.0053** **Imazalil 0.13** **Oxydemeton-methyl (sum) 0.0014**
Comments: For exposure calculation of the pesticides the Danish exposure figures from the recent publication of Jensen et al. (2015) are used.					
Human biomonitoring: The urinary excretion of DAPs, with are metabolites of organophosphate pesticides such as Chlorpyrifos, have been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that the organophosphate metabolites could be detected in nearly all samples.					

References:

Jensen BH, Petersen A, Nielsen E, Christensen T, Poulsen ME, Andersen JH. Cumulative dietary exposure of the population of Denmark to pesticides. Food Chem Toxicol. 2015 Sep; 83: 300-7.

Phenolic compounds

<table>
<tr><th colspan="6">Bisphenol A</th></tr>
<tr><th>Selected References</th><th>Source of exposure</th><th>Exposure</th><th>Further calculations/ modifications</th><th>Mean exposure (oral, dermal, inhal, intern)</th><th>Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)</th></tr>
<tr><td>EFSA 2015b</td><td>Food
Dust
Air
Cosmetics
Other consumer products</td><td>Food:
Women: 18-45 years:
Average: 132 ng/kg/d (o)
High: 388 ng/kg/d (o)

Total exposure (food, dust, thermal paper, cosmetics):
Women 18-45 years:
Average: 216 ng/kg/d (int)
High: 1066 ng/kg/d (int)</td><td>For internal dose estimation the following absorption rates are used:
100 % absorption for both ingestion and inhalation, 10 % for dermal absorption of BPA from thermal paper and 50 % for dermal absorption of BPA from cosmetics</td><td>132 ng/kg/d (o, int)

216 ng/kg/d (int)</td><td>388 ng/kg/d (o, int)

1066 ng/kg/d (int)</td></tr>
<tr><td>ECHA/RAC 2015</td><td>Air
Dust
Food

Thermal receipts</td><td>Table 42. Internal doses (ID) associated with other media than thermal paers: air, settled dust and food exposure media, for pregnant women and their unborn child.
<table><tr><th rowspan="2">Exposure scenario</th><th colspan="2">Internal exposure dose by µg.kg^{-1}.d^{-1}</th></tr><tr><th>median</th><th>95th percentile</th></tr><tr><td>Exposure by inhalation</td><td>1.63.10^{-4}</td><td>6.8.10^{-4}</td></tr><tr><td>Exposure by ingestion of settled dust</td><td>6.23.10^{-5}</td><td>2.07.10^{-4}</td></tr><tr><td>Exposure by ingestion of food and beverages</td><td>1.36.10^{-3}</td><td>3.8.10^{-3}</td></tr><tr><td>Total exposure resulting from the aggregation of these three routes of exposure</td><td>1.68.10^{-3}</td><td><b>4.18.10^{-3}</td></tr></table>Calculation of internal doses is based on a consideration of knowledge on the absorption or bioavailability of BPA in the body. On the basis of a critical analysis of the available toxicokinetic data, the bioavailability factor used by oral route of unconjugated BPA is 3% and by inhalation is 100%. For dermal absorption a factor of 10% or dermal penetration rates are used.

pregnant women consumers handling thermal receipts</td><td>Total internal exposure
1.68 ng/kg/d (int)

10 ng/kg/d (int)</td><td>Total internal exposure
4.18 ng/kg/d (int)

80 ng/kg/d (int)</td></tr>
</table>

		10 ng/kg/d median (int) 80 ng/kg/d 95-perct (int) 260 ng/kg/d worst-case (int)		**260 ng/kg/d worst-case (int)**
Aggregated exposure taken forward in evaluation:			***216* ng/kg/d (int)**	**1066 ng/kg/d (int)**
Comments: For internal exposure calculations ECHA/RAC used and an oral absorption rate of 3%, whereas EFSA used an absorption rate of 100% which very much affect the internal dose calculation. The data from EFSA 2015 updated data of high quality and the total exposure estimates are based on this report. In the Danish database on consumer product many products containing bisphenol A are found, with the highest exposure potential from baby dummies/pacifiers and thermal paper. It should be noted that exposure data given in Danish EPA 2009 and Danish EPA 2012 regarding exposure to toddlers and pregnant women are not further used as more recent data on the dominating exposure sources food and thermal paper is available from the evaluations by ECHA/RAC 2015 and EFSA 2015.				
Human biomonitoring: Bisphenol A has been measured several times in Danish children and women and widespread exposure is documented. Exposure calculations has been made to estimate the exposure levels by Frederiksen et al. (2013b) based on the urinary excretion levels of bisphenol A . The calculated exposure levels are similar to or lower compared to the estimated exposure presented in the present table: mean 0.03-0.04 µg/kg bw/d, 95-perc: 0.13-0.24 µg/kg bw/d (Frederiksen 2013b). EFSA 2015 noted by comparing estimated internal exposure with biomonitoring data, the forward modelling approach gave about 4-fold higher estimates (42–387 vs. <10–107 ng/kg bw per day) than the biomonitoring approach for average exposure, and about 2-fold higher for high exposure, demonstrating quite a good agreement between these two approaches.				

References:

ECHA/RAC 2015. Background document to the Opinion on the Annex XV dossier proposing restrictions on 4.4'-isopropylidenediphenol (Bisphenol A; BPA) ECHA/RAC/RES-O-0000001412-86-56/F. Committee for Risk Assessment (RAC); Committee for Socio-economic Analysis (SEAC). 11 Sept. 2015.

EFSA 2015: Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids. EFSA Journal 2015;13(1):3978

Frederiksen et al., 2013b. Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. 2013 Nov;216(6):772-83

Bisphenol F

Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Liao 2013	Food Based on measurements of beverages, dairy products, fats and oils, fish and seafood, cereals, meat and meat products, fruits, vegetables and others Paper	Dietary intake: Adults Mean: 7.46 ng/kg bw/d 95-perc: 19.7 ng/kg bw/d		7.46 ng/kg bw/d (o)	19.7 ng/kg bw/d (o)
Aggregated exposure taken forward in evaluation:				**7.46 ng/kg bw/d (o)**	**19.7 ng/kg bw/d (o)**

Comments: The exposure estimates for Bisphenol F are based on the exposure estimates from an American research paper, with US measurements. All though there may be continental differences, the estimated exposures are considered relevant for the present project as more local data are missing.
Human biomonitoring: No human biomonitoring study within the identified criteria was found.

References:

Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. Agric Food Chem. 2013 May 15;61(19):4655-62

Bisphenol S

Selected References	Source of exposure	Exposure	Further calculations/ modifications	Mean exposure (oral, dermal, inhal, intern)	Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)
Liao 2013	Food Based on measurements of beverages, dairy products, fats and oils, fish and seafood, cereals, meat and meat products, fruits, vegetables and others Paper	Dietary intake: Adults Mean: 1.31 ng/kg bw/d 95-perc: 1.66 ng/kg bw/d		1.31 ng/kg bw/d (o)	1.66 ng/kg bw/d (o)
Aggregated exposure taken forward in evaluation:				**1.31 ng/kg bw/d (o)**	**1.66 ng/kg bw/d (o)**
Comments: The exposure estimates for Bisphenol F are based on the exposure estimates from an American research paper, with US measurements. All though there may be continental differences, the estimated exposures are considered relevant for the present project as more local data are missing.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References:

Liao C, Kannan K. Concentrations and profiles of bisphenol A and other bisphenol analogues in foodstuffs from the United States and their implications for human exposure. Agric Food Chem. 2013 May 15;61(19):4655-62.

Nonylphenol					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Gyllenhammar 2012	Food	Mean intake of 27.2 µg/day (range 14-40)	Adult of 60 kg	0.45 µg/kg bw/d (o)	0.67 µg/kg bw/d (o)
MST 2012	Food Dust Air Clothing	Dietary exposure (internal) Adults: 0.2 µg/kg bw/d Indoor air/dust (internal): Median: 0.0277 µg/kg bw/d Maximum: 0.1057 µg/kg bw/d Consumer products (internal): Mean: 4.5281 µg/kg bw/d Maximum: 9.05630 µg/kg bw/d		Dietary exposure (internal) 0.2 µg/kg bw/d (o) Indoor air/dust (internal): 0.0277 µg/kg bw/d (inh/o) Consumer products (internal): 4.5281 µg/kg bw/d (d)	Dietary exposure (internal) 0.2 µg/kg bw/d (o) Indoor air/dust (internal): 0.1057 µg/kg bw/d (inh/o) Consumer products (internal): 9.05630 µg/kg bw/d (d)
MEFD 2016		Limit values: Drinking water: 20 µg/l	0.014 L/kg/d water ingestion of pregnant women (mean) 0.043 L/kg/d water ingestion of pregnant women (95-perc)	Drinking water: 0.28 µg/kg bw/d (o)	Drinking water: 0.83 µg/kg bw/d (o)
Aggregated exposure taken forward in evaluation (total internal exposure, oral, inh and dermal):				**4.8µg/kg bw/d (total int)**	**9.4µg/kg bw/d (total int)**
Comments: The data from MST 2012a contain data considered sufficient for making exposure estimates for pregnant women in this project. Gyllenhammar et al reached similar dietary exposure levels. As the MST report has calculated a sufficient and conclusive total internal exposure, this level is taken forward for the risk assessment.					
Human biomonitoring: No human biomonitoring study within the identified criteria was found.					

References.

Gyllenhammar I, Glynn A, Darnerud PO, Lignell S, van Delft R, Aune M. 4-Nonylphenol and bisphenol A in Swedish food and exposure in Swedish nursing women. Environ Int. 2012 Aug;43:21-8.

MST 2012: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Phthalates

DEHP (di-ethyl-hexyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Consumer products (articles) Indoor env. Food	Basic scenarios (BS as average and maximum) and specific worst case scenario were estimated for pregnant women based on content and exposure to the various sources	Basic scenario:		
		Articles: BS (average-max): 0.81- 2.03 µg/kg/d	Articles	0.81 µg/kg/d (int)	2.03 µg/kg/d (int)
		Indoor env: BS (average-max): 0.21-2.78 µg/kg/d		0.21 µg/kg/d (int)	2.78 µg/kg/d (int)
		Food: BS (average-max): 1.20- 2.20 µg/kg/d		1.20 µg/kg/d (int)	2.20 µg/kg/d (int)
		BS, Sum (average-max): 2.22- 7.01 µg/kg/d		2.22 µg/kg/d (int)	7.01 µg/kg/d (int)
		Specific Worst Case Sscenario, (average-max): 12.1 -24.2 µg/kg/d	Specific worst case scenario: Exposure from using plastic sandals and migration of phthalate into a sunscreen treated foot.	**12.1 µg/kg/d (int)**	**24.2 µg/kg/d (int)**
ECHA 2016	Various articles Indoor env Food	Women, articles: Median: 2.12 µg/kg/d Worst case: 7.63µg/kg/d	Articles	**2.12 µg/kg/d (int)**	**7.63 µg/kg/d (int)**
		Womwn, indoor env.: Median: 0.48 µg/kg/d Worst case: 2.52 µg/kg/d	Indoor env.	**0.48 µg/kg/d (int)**	**2.52 µg/kg/d (int)**
		Women, food: Median: 1.49t given Worst case: 2.86 µg/kg/d	Food	**1.49 µg/kg/d (int)**	**2.86 µg/kg/d (int)**
			Sum, EU data	**4.09 µg/kg/d (int)**	**13,01 µg/kg/d (int)**

		Danish biomonitoring, DEMOCOPHES project, women: Median: 1.61 µg/kg/d 95-perc: 5.37 µg/kg/d	NB: Danish exposure values from biomonitoring about 80% of the Danish estimated exposure from Danish EPA 2012.	1.61 µg/kg/d (int)	5.37 µg/kg/d (int)
DBP (di-butyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Consumer products (articles) Indoor env. Food	Basic scenarios (BS as average and maximum) and specific worst case scenario were estimated for pregnant women based on content and exposure to the various sources	Basic scenario:		
		Articles: BS (average-max): 0.72- 1.45 µg/kg/d	Articles	0.72 µg/kg/d (int)	1.45 µg/kg/d (int)
		Indoor env: BS (average-max): 0.058-0.46 µg/kg/d	Indoor env.	0.058 µg/kg/d (int)	0.46 µg/kg/d (int)
		Food: BS (average-max): 0.26- 1.40 µg/kg/d	Food	0.26 µg/kg/d (int)	1.40 µg/kg/d (int)
		BS, Sum (average-max): 1.04- 3.30 µg/kg/d	About a factor 2 higher than biomonitoring data below!	1.04 µg/kg/d (int)	3.30 µg/kg/d (int)
ECHA 2016	Various articles Indoor env Food	**Specific worst case scenario, (average-max): 0.72 -1.45 µg/kg/d**	Specific worst case scenario: Exposure from using plastic sandals and migration of phthalate into a sunscreen treated foot.	**0.72 µg/kg/d (int)**	1**.45 µg/kg/d (int)**
		Women: Articles: Median: 0.74 µg/kg/d Worst case: 2.56 µg/kg/d	Articles	0**.74µg/kg/d (int)**	**2.56 µg/kg/d (int)**
		indoor env.: Median: 0.02 µg/kg/d Worst case: 0.12 µg/kg/d	Indoor env.	**0.02 µg/kg/d (int)**	**0.12 µg/kg/d (int)**
		Food: Median: 0.08 µg/kg/d Worst case: 97.5 perc: 0.16 µg/kg/d	Food	**0.08 µg/kg/d (int)-**	**0.16 µg/kg/d (int)**
			Sum, EU data	**0.84 µg/kg/d (int)**	**2.92 µg/kg/d (int)**

		Danish , biomonitoring, DEMOCOPHES project, women: Median: 0.66 µg/kg/d 95-perc: 1.28 µg/kg/d	NB: Danish exposure values from biomonitoring about 40-60% of Danish estimated exposure from Danish EPA 2012.	0.66 µg/kg/d (int)	1.28 µg/kg/d (int)
DIBP (di-iso-butyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Consumer products (articles) Indoor env. Food	Basic scenarios (BS as average and maximum) and specific worst case scenario were estimated for pregnant women based on content and exposure to the various sources	Basic scenario:		
		Articles: BS (average-max): 3.00- 6.00 µg/kg/d	Articles	3.00 µg/kg/d (int)	6.00 µg/kg/d (int)
		Indoor env: BS (average-max): 0.038-2.25 µg/kg/d	Indoor env	0.038 µg/kg/d (int)	2.25 µg/kg/d (int)
		Food: BS (average-max): 0.60- 2.10 µg/kg/d	Food	0.60 µg/kg/d (int)	2.10 µg/kg/d (int)
		BS, Sum (average-max): 3.64- 7.01 µg/kg/d		3.64 µg/kg/d (int)	10.4 µg/kg/d (int)
		Specific worst case scenario, (average-max): 6.73 -13.5 µg/kg/d	Specific worst case scenario: Exposure from using plastic sandals and migration of phthalate into a sunscreen treated foot.	**6.73 µg/kg/d (int)**	**13.5 µg/kg/d (int)**
ECHA2016	Various articles Indoor env Food	Women Articles: Median: 0.65 µg/kg/d Worst case: 2.34 µg/kg/d	Articles	**0.65 µg/kg/d (int)**	**2.34µg/kg/d (int)**
		Indoor env.: Median: 0.02 µg/kg/d Worst case: 0.11 µg/kg/d	Indoor env.	**0.02 µg/kg/d (int)**	**0.11 µg/kg/d (int)**
		Food: Median: 0.14 Worst case: 0.28 µg/kg/d	Food	**0.14 µg/kg/d (int)**	**0.28 µg/kg/d int**

			Sum, EU data	**0.82µg/kg/d (int)**	**2.74 µg/kg/d (int)**
		Danish , biomonitoring, DEMOCOPHES project, women: Median: 1.22 µg/kg/d 95-perc: 3.30 µg/kg/d	NB: Danish exposure values from biomonitoring about 30% of Danish estimated exposure from Danish EPA 2012.	1.22 µg/kg/d (int)	3.30 µg/kg/d (int)
BBP (butyl-benzyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Consumer products (articles) Indoor env. Food	Basic scenarios (BS as average and maximum) and specific worst case scenario were estimated for pregnant women based on content and exposure to the various sources	Basic scenario:		
		Articles: BS (average-max): 0 µg/kg/d	Articles	0 µg/kg/d (int)	0 µg/kg/d (int)
		Indoor env: BS (average-max): 0.015-0.25 µg/kg/d	Indoor env	0.015 µg/kg/d (int)	0.25 µg/kg/d (int)
		Food: BS (average-max): 0.20- 0.40 µg/kg/d	Food	0.20 µg/kg/d (int)	0.40 µg/kg/d (int)
		BS, Sum (average-max): 0.22- 0.65 µg/kg/d		0.22 µg/kg/d (int)	0.65 µg/kg/d (int)
		No exposure of BBP from use of plastic sandals used for specific worst case scenario for other phthalates	About 50% higher levels compared to biomonitoring data.	-	-
ECHA2016	Various articles Indoor env Food	Women Median: 0.19µg/kg/d Worst case: 0.68 µg/kg/d	Articles	**0.19 µg/kg/d (int)**	**0.68 µg/kg/d (int)**
		Adults, indoor env.: Median: 0.01µg/kg/d Worst case: 0.0.3 µg/kg/d	Indoor env.	**0.01 µg/kg/d (int)**	**0.03 µg/kg/d (int)**
		Adults, food: Median: 0.05 µg/kg/d (int)n Worst case : 0.12 µg/kg/d	Food	**0.05 µg/kg/d (int)**	**0.12 µg/kg/d (int)**

			Sum, EU data	**0.25 µg/kg/d (int)**	**0.83 µg/kg/d (int)**
		Danish , biomonitoring, DEMOCOPHES project, women: Median: 0.13 µg/kg/d 95-perc: 0.52 µg/kg/d	NB: Danish exposure values from biomonitoring in the same range as the Danish estimated exposure from Danish EPA 2012.	0.13 µg/kg/d (int)	0.52 µg/kg/d (int)
DINP (di-iso-nonyl-phthalate)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Consumer products (articles) Indoor env. Food	Basic scenarios (BS) for pregnant women based on content and exposure to the various sources			
		Articles: BS (average-max): no data	Articles	**0 µg/kg/d (int)**	**0 µg/kg/d (int)**
		Indoor env: BS (average-max): 0.017-0.80 µg/kg/d	Indoor Env	**0.017 µg/kg/d (int)**	**0.80 µg/kg/d (int)**
		Food: BS (average-max): 0.45- 1.40 µg/kg/d	Food	**0.45 µg/kg/d (int)**	**1.40 µg/kg/d (int)**
		BS, Sum (average-max): 0.47- 2.20 µg/kg/d	Danish biomonitoring data above about a factor 2 higher (see below)	**0.47 µg/kg/d (int)**	**2.20 µg/kg/d (int)**
Dipentyl phthalatee					
No data found					
Di-n-hexyl phthalate					
No data found					
DnOP (Di-n-octyl phthalate)					
Sakhi et al. 2014	Food	Based on analytical content in food items population exposure (adults) were made for the Norwegian population: Adults Median: 0.022 µg/kg/d 95-perc: 0.063 µg/kg/d		**0.022 µg/kg/d (int)**	**0.063 µg/kg/d (int)**

Sioen et al. 2012	Food	Estimated intake based in content in food and intake of food in Belgium Adults Average intake Median: 0.015 µg/kg/d 95-perc: 0.030 µg/kg/d High intake Median: 0.062 µg/kg/d 95-perc: 0.130 µg/kg/d	The Norwegian values are preferred and also fit into the ranges of average and high exposure from the Belgian data		
Di-cyclo-hexyl-phthalate (DCHP)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Sakhi et al. 2014	Food	Based on analytical content in food items population exposure (adults) were made for the Norwegian population: Adults Median: 0.016 µg/kg/d 95-perc: 0.031 µg/kg/d		**0.016 µg/kg/d (int)**	**0.031 µg/kg/d (int)**
Sioen et al. 2012	Food	Estimated intake based in content in food and intake of food in Belgium Adults Average intake Median: 0.019 µg/kg/d 95-perc: 0.042 µg/kg/d High intake Median: 0.076 µg/kg/d 95-perc: 0.156 µg/kg/d	The Norwegian data preferred over Belgium data although exposure estimates is a factor 2-5 lower than the Belgian estimates		
di-2-propylheptyl phthalate (DPHP)					
No data found					

Comments

For DEHP, DBB. DiBP and BBP the data from exposure modelling in the recent ECHA 2016 document is considered the most adequate data set for exposure estimations of today and thus chosen for further risk assessment. DiNP exposure estimates are based on the Danish data sources Dansih EPA (2012). In relation to biomonitoring data the exposure estimates chosen for further risk assessment are based on Danish biomonitoring data (Frederiksen et al. 2013, see below) as these data are the original data for the estimations provided by ECAH 2016 for Danish women. . Exposure estimates regarding DnOP and DCHP are based on recent Norwegian estimates based on analytical content in food and consumption data, i.e. other sources than food is not included for these substances.

It was not possible due to lack of data to provide exposure estimates for dipentylphthalate, di-n-hexylphthalate and di-2-propylheptyl phthalate.

Human biomonitoring: The urinary phthalate concentrations have been measured several Danish studies of Danish children adult women/pregnant women. Exposure calculations have been performed for both children and mothers/women. For the women the following values are found for the phthalates:
DEHP (median: 1.56 µg/kg/d 95p: 5.12 µg/kg/d),
DBP (median: 0.543 µg/kg/d 95p: 1.34 µg/kg/d),
DiBP (median: 1.66 µg/kg/d 95p: 5.21 µg/kg/d),
BBP (median: 0.13 µg/kg/d 95p: 0.47 µg/kg/d)
DiNP (median: 0.75 µg/kg/d 95p: 5.50 µg/kg/d).
The estimated exposure based on biomonitoring data are generally lower compared to EPA and ECHA evaluations.
For the majority of the phthalates the exposure seems higher in children compared to adults, except for MEP, which is a phthalate often found in cosmetics (Frederiksen 2013). The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population.

References

Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Survey of chemical substances in consumer products no. 117. Danish EPA.
ECHA 2016. ANNEX XV RESTRICTION REPORT. PROPOSAL FOR A RESTRICTION SUBSTANCE NAMES: FOUR PHTHALATES (DEHP, BBP, DBP, DIBP).
Frederiksen et al. (2013).Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. Nov;216(6):772-83.
Sakhi AK et al. (2014). Concentrations of phthalates and bisphenol A in Norwegian foods and beverages and estimated dietary exposure in adults. Environ Int. Dec;73:259-69.
Sioen et al. (2012) Phthalates dietary exposure and food sources for Belgian preschool children and adults. Environ Int. Nov 1;48:102-8.

UV-filters

Benzophenone 3 (BP-3)					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012 Danish EPA 2015	Cosmetics	Up to 10% in sunscreen. Typical scenario: Use of 18 g sunscreen/d results in exposure of 30 mg/kg/d or 1.2 mg/kg/d as internal dose Worst case: Use of 2 x 18 g sunscreen/d results in exposure of 60 mg/kg/d A specific absorption rate of **4% was used by** Danish (EPA 2012). Default value of 10% used in Danish EPA (2015). SCCS 2008 indicate a mean dermal absorption of 3.1% and uses a value of 9.9% as an upper level).	For the purpose of this project the exposure estimates will be adjusted according to the recent adopted maximum level of 6% in sunscreen. : 18 g x 0.06 g /g x 0.04 / 60 kg = 0.72 mg/kg/d 2 x. 18 g x 0.06 g /g x 0.04 / 60 kg = 1.4 mg/kg/d A dermal absorption rate of 4% is considered the best estimate as an overall dermal absorption rate for the whole exposed body surface area.	30 mg/kg/d (d) 0.72 mg/kg/d (int)	60 mg/kg/d (d) 1.4 mg/kg/d (int)
2-ethylhexyl 4-methoxycinnamate (OMC)					
Danish EPA 2012 Danish EPA 2015	Cosmetics	Up to 10% in sunscreen. Typical scenario: Use of 18 g sunscreen/d results in exposure of 30 mg/kg/d Worst case: Use of 2 x 18 g sunscreen/d results in exposure of 60 mg/kg/d Specific absorption rate of **2%** (Danish EPA 2012). Default value of 10% used in Danish EPA (2015). SCCNFP (2001) used a dermal absorption rate of 2%.	A dermal absorption factor of 2%	**30 mg/kg/d (d)** **0.6 mg/kg/d (int)**	**60 mg/kg/d (d)** **1.2 mg/kg/d (int)**
Comments: Only BP-3 and 2-ethylhexyl 4-methoxycinnamate are allowed for use as UV-filters in cosmetics. No data on exposure from BP-2 and only minute exposure from BP-1 could be expected.					

Human biomonitoring: Human biomonitoring of the UV-filter BP-3 have been performed in two Danish studies of Danish children adult women and document wide exposure to this particular filter. Exposure calculations were performed for children 6-10 years of age (mean: 26.7 ng/kg bw/d, 95p: 1388 ng/kg bw/d). The calculated mean exposure of BP-3 is lower compared to values presented by the Danish EPA. The biomonitoring studies were not conducted specifically on people using sunscreen, and were performed during fall and winter seasons.

References:

Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Survey of chemical substances in consumer products no. 117. Danish EPA.

Danish EPA (2015). Survey and health assessment of UV filters. Survey of chemical substances in consumer products no. 142. Danish EPA.

SCCS (2008). SCCP OPINION ON Benzophenone-3 Scientific Committee on Consumer Products. SCCP/1201/08

SCCNFP (2001). Opinion on the Evaluation of Potentially Estrogenic Effects of UV-filters adopted by the SCCNFP during the 17th Plenary meeting of 12 June 2001 http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/sccnfp_opinions_97_04/sccp_out145_en.htm

Other substances

Acrylamide					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
EFSA 2015	Food	Total dietary exposure: Median: Adults: 0.5 µg/kg/d 95-percentiles: Adults: 1.0 µg/kg/d		**0.5 µg/kg/d (o)**	**1.0 µg/kg/d (o)**
MEFD 2016	Drinking water	Limit value: 0.1 µg/L	0.014 L/kg/d water ingestion, pregnant women (mean) 0.043 L/kg/d water ingestion, pregnant women (95-perc)	0.0014 µg/kg/d (o) Insignificant exposure compared to food exposure	0.0043 µg/kg/d (o) Insignificant exposure compared to food exposure
Aggregated exposure taken forward in evaluation:				**0.5 µg/kg/d (o)**	**1.0 µg/kg/d (o)**
Comments: No other relevant sources for exposure could be found. A potential drinking water contribution is considered insignificant. The exposure estimates are considered as reliable.					
Human biomonitoring: No applicable human biomonitoring study was found in adults; however, a biomonitoring study from Germany (Heudorf et al., 2009) has estimated the level of exposure in 5-6 year old German children based on urinary measurements of acrylamide metabolites, and found levels similar to the present exposure estimations (mean: 0.54 µg/kg bw/d.; 95-perc: 1.91 µg/kg bw/d).					

References

EFSA (2015). EFSA opinion on acrylamide in food. EFSA Journal 2015;13(6):4104.

Heudorf et al (2009) Acrylamide in children – exposure assessment via urinary acrylamide metabolites as biomarkers. Int. J. Hyg. Environ. Health 212: 135–141

MEFD (2016). Ministry of Environment and Food of Denmark. Bekendtgørelse nr 802 af 1. Juni 2016, Bekendtgørelse om vandkvalitet og tilsyn med vandforsyningsanlæg.

Siloxane D4					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
MST 2012	Cosmetics	Internal exposure doses: Basic scenario (body lotions) Mean: 0.003 µg/kg bw/d High: 0.005 µg/kg bw/d Scenario using sunscreen Mean: 10.2 µg/kg bw/d High: 20.4 µg/kg bw/d	Dermal absorption rate 1% Concentration in cosmetics 0,0003% and in sunscreen 0.34%	Cosmetic products other than sunscreens: **0.003 µg/kg bw/d** (int, after dermal uptake)) Sunscreens 10.2 µg/kg bw/d (int, after dermal uptake)	Cosmetic products other than sunscreens: 0.005 µg/kg bw/d (int, after dermal uptake) Sunscreens **20.4 µg/kg bw/d** (int, after dermal uptake)
SCCS 2010	Cosmetics	Cosmetic products other than sunscreens: 100 µg/kg bw/d (Systemic exposure dose) Sunscreens: 100 µg/kg bw/d (Systemic exposure dose)	Dermal absorption rate 0.5% Concentration in cosmetics/sunscreen 7.8% Worst case was calculated as exposure without sunscreen plus exposure with sunscreen.	Cosmetic products other than sunscreens: 100 µg/kg bw/d (int, after dermal uptake)	Including Sunscreens: 200 µg/kg bw/d (int, after dermal uptake)
Pieri 2013	Indoor air	Average daily intake based on the sum of 6 siloxane in samples from different indoor environments in UK and Italy. UK adults: 1875 µg/d Italy adults: 1563 µg/d No specific calculations were made for D4.		No specific calculations were made for D4.	No specific calculations were made for D4.
Comments: The exposure assessments on D4 in the reports by MST 2012 and SCCS 2010 did not reach similar levels of exposure. The reason for the discrepancy is the different amount of D4 assumed to be in the cosmetic products. The values from the Danish evaluation are used, and for mean exposure the exposure from cosmetic products other than sunscreens are used, whereas the use of sunscreen is added to the high exposure scenario. The SCCS data is used for a special (worst case) estimation. The study from Italy (by Pieri) calculated the potential exposure from indoor air, however, the estimates were based on a total of 8 siloxanes and therefore no specific estimates are available for D4. The study shows that exposure from indoor air may be an important contributor to the total siloxane exposure.					
Human biomonitoring: No human biomonitoring study within the identified criteria were found					

References:
MST 2012a: Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117, 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende
SCCS 2010: Scientific Committee on Consumer Safety OPINION ON Cyclomethicone. SCCS/1241/10

Pieri F, Katsoyiannis A, Martellini T, Hughes D, Jones KC, Cincinelli A. Occurrence of linear and cyclic volatile methyl siloxanes in indoor air samples (UK and Italy) and their isotopic characterization. Environ Int. 2013 Sep;59:363-71.

Triclosan					
Selected References	**Source of exposure**	**Exposure**	**Further calculations/ modifications**	**Mean exposure (oral, dermal, inhal, intern)**	**Worst-case/ 95-perct. Exposure (oral, dermal, inhal, intern)**
Danish EPA 2012	Cosmetics Dust	Pregnant women: Dust (µg/kg bw/day): Mean: 0.0015, high 0.0002 Cosmetics (toothpaste / deodorant at max concentration of 0.3%) Only toothpaste: 7.3 µg/kg/day Both (high exp.): 22 µg/kg/day	Dust not further considered as exposure is marginal compared to cosmetics.	**7.3 µg/kg/day (oral)**	**22 µg/kg/day (oral)**
SCCP 2009	Cosmetics	Adults: 36 µg/kg/d Four common-use products having a triclosan content if 0.3% Adults: 300 µg/kg/day Eight products with current content of triclosan	For worst case exposure when using all product categories the current content of triclosan is used. If a max content of 0.3% is used the exposure is 526 µg/kg/day: However such a scenario seems unrealistic considering the Danish findings on triclosan in cosmetics (see below).	36 µg/kg/d (int)	300 µg/kg/day (int)
Comments: A Danish survey from 2006 indicated that only very few cosmetic products contained triclosan. Therefore, the Danish exposure estimate is considered most realistic, and for Danish conditions the SCCP estimate is considered too extreme. There is no data found for potential exposure from other sources, however, such exposure most likely would be very low compared to the exposure from cosmetics.					
Human biomonitoring: The urinary triclosan concentrations have been measured in several Danish studies of Danish children adult women/pregnant women. The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population. Exposure calculations have not been performed on measurements from the Danish population, however, a study from Belgium estimated the exposure in obese adults to be 490 ng/kg bw/d (90-perc: 565 ng/kg bw/d)(Geens 2015). The calculated exposure estimations, based on the urinary excretion of triclosan are lower compared to the exposure levels estimates from the Danish EPA.					

References:

Danish EPA (2012). Exposure of pregnant consumers to suspected endocrine disruptors. Kortlægning af kemiske stoffer i forbrugerprojekter nr. 117. Miljøstyrelsen.
Geens et al. (2015). Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals. Environ Int. 2015 Mar;76:98-105.
SCCP (2009) Scientific Committee on Consumer Products, Opinion on triclosan, SCCP/1192/08

Appendix 6c

Human biomonitoring studies

The table below lists the relevant human biomonitoring studies that have been identified for the estimation of exposure to the respective compounds.
The list covers all identified recent Danish studies as well as other recent studies where relevant exposure estimates have been performed. Estimated exposure values in bold are taken forward in the evaluation and are included in tables 6.1-6.4 in the report.

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
Acrylamide						
Acrylamide	Heudorf 2009	Germany, 5-6 year old children (n=110)	Urine measurements of Acrylamide metabolites AAMA and GAMA	36.0 (152.7) mg AAMA/L urine 13.4 (55.9) mg GAMA/L urine	**0.54 µg/kg bw/d**	**1.91 µg/kg bw/d**
	Comments: The estimated levels of exposure based on urinary measurements of acrylamide metabolites in German children are somewhat lower compared to the exposures estimated by EFSA (2015) and presented in the present project.					
	References: *Heudorf et al., 2009. Acrylamide in children – exposure assessment via urinary acrylamide metabolites as biomarkers. Int. J. Hyg. Environ. Health 212: 135–141*					
Aluminium						
Aluminium	No relevant human biomonitoring studies were found.					
BHA/BHT						
BHA	No relevant human biomonitoring studies were found.					
BHT	No relevant human biomonitoring studies were found.					
Bisphenols						
Bisphenol A	Frederiksen 2013a	Denmark: Children and adolescents (n=129)	Urine (24 h samples)	1.37 (8.60) ng/mL	Children (6-10y): **0.066 µg/kg** bw/d	Children (6-10y): **0.283 µg/kg bw/d**
	Frederiksen 2013b	Denmark: Children 6-11 years Adult women (n=290)	Urine (morning spot)	Children: 1.7 (7.9) ng/mL Women: 2.1 (11) ng/mL	Children**: 0.04 µg/kg bw/d** Women: **0.03-0.04 µg/kg bw/d**	Children**: 0.15**-0.22 µg/kg bw/d Women: **0.13-0.24 µg/kg bw/d**
	Covaci 2015	Denmark and 6 other EU countries: Children 6-11 years	Urine (morning spot)	Children: 1.96 (13.14) ng/mL Women: 1.94 (11.13) ng/mL	Geometric mean (95% CI) 0.036 ng/kg bw/d: Belgium	

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
		(n=653) Adult women (n=639)			Children: 41.2 (32.9–51.7) Women: 39.5 (33.3–46.8) Denmark Children 38.9 (32.2–47.0) Women 35.7 (29.9–42.6) Luxembourg Children: 35.2 (27.3–45.3) Women: 30.0 (24.7–36.3) Slovenia Children: 41.4 (31.7–54.2) Women: 18.1 (13.2–24.7) Spain Children: 38.3 (31.4–46.7) Women: 32.7 (26.8–39.8) Sweden Children: 32.6 (27.8–38.3) Women: 21.2 (18.7–24.1)	
	Comments: Bisphenol A has been measured several times in Danish children and women and widespread exposure is documented. Exposure calculations have been made to estimate the exposure levels. The Data from Frederiksen 2013b from Denmark is also included in Covaci 2015. The calculated exposure levels are lower than the estimated exposure in the present report based on EFSA and Danish EPA reports.					
	References: *Covaci A et al., 2015. Urinary BPA measurements in children and mothers from six European member states: Overall results and determinants of exposure. Environ Res. 2015 Aug;141:77-85* *Frederiksen et al., 2013a. Bisphenol A and other phenols in urine from Danish children and adolescents analyzed by isotope diluted TurboFlow-LC-MS/MS. Int J Hyg Environ Health. 2013 Nov;216(6):710-20.* *Frederiksen et al., 2013b. Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. 2013 Nov;216(6):772-83.*					
Bisphenol F	No relevant human biomonitoring studies were found.					
Bisphenol S	No relevant human biomonitoring studies were found.					
Brominated flame retardants						
PBDEs	Vorkamp (2009)	Denmark Pregnant women, Odense child cohort (n=100)	Serum	Deca-BDE (BDE-209): 46 (Max: 464) pg/mL Penta-DBE BDE-47: 19 (max: 64) pg/mL	No exposure calculations	No exposure calculations

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
				BDE-99): 14 (max: 42) pg/mL		
	Schlumpf (2010)	Human breast milk from Swiss mothers 2004-2006	Human milk		Breast fed infants: Median: BDE-47: **0.009 µg/kg/d** BDE-99: **0.003 µg/kg/d**	Breast fed infant: Max: BDE-47: **0.1 µg/kg/d** BDE-99: **0.043 µg/kg/d**
	Comments: The levels of poly brominated flame retardants has been measured several times in Danish children and women. Exposure calculations have been performed for infants based on measurements in human milk.					
	References: *Vorkamp et al (2009). Polybrominated Diphenyl Ethers and Perfluoroalkyl Substances in Serum of Pregnant Women: Levels, Correlations, and Potential Health Implications. Arch Environ Contam Toxicol 67:9–20* *Schlumpf M, Kypke K, Wittassek M, Angerer J, Mascher H, Mascher D, Vökt C, Birchler M, Lichtensteiger W. Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere. 2010 Nov;81(10):1171-83.*					
Chlorinated solvents						
Tetrachloroethylene	No relevant human biomonitoring studies were found.					
Hydrocarbons						
n-hexane, various isomers of C7 – C12 hydrocarbons	No relevant human biomonitoring studies were found.					
Lead						
Lead and substances	No relevant human biomonitoring studies were found.					
Mercury						
Mercury	Mørck (2015)	Denmark: Children 6-11 years (n=144) Women (n=145)	Hair	Geometric mean (95% CI): Children: 0.249 (0.219–0.284) µg/g hair Women: 0.420 (0.368–0.479) µg/g hair Maximum: Children: 1.335 µg/g hair Mothers: 2.822 µg/g hair	No exposure calculations	No exposure calculations
	Comments:					

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
	The levels of mercury has been measured the hair of Danish children and their mothers. Exposure calculations have not been performed, but the intake of fish was significantly associated mercury concentrations in hair. The level of mercury in hair also increased with age in the women.					
	References: *Mørck et al (2015a). The Danish contribution to the European DEMOCOPHES project: A description of cadmium, cotinine and mercury levels in Danish mother-child pairs and the perspectives of supplementary sampling and measurements. Environmental Research 141 (2015) 96–105*					
Nonylphenol						
Nonylphenol	No relevant human biomonitoring studies were found.					
Organophosphate flame retardants						
TCEP	No relevant human biomonitoring studies were found.					
Parabens						
Propylparaben, butylparaben	Frederiksen (2013b)	Denmark: Children 6-11 years (n=144) Women (n=145)	Urine (morning spot)	**n-propylparaben:** Children, detected in 46%: mean: 2.0 ng/mL, 95-perc: 14 ng/mL Mothers. detected in 83%: Mean: 10 ng/mL Median (95-perc): 1.7 (33) ng/mL, **n-butylparaben:** Children: detected in 17%: Mean: 0.19 ng/mL 95-perc: 1.4 ng/mL, Mothers detected in 39%: Mean: 9.3 ng/mL 95-perc: 1.8 ng/mL	No exposure calculations	No exposure calculations
	Frederiksen (2014)	Overview of several Danish studies in Denmark: Children and pregnant women	Urine (morning spot), 24 h urine samples	Median paraben levels: <1–12 ng/ml **n-Propylparaben** maximum: Children: 2.2 mg/ml Pregnant women: 646 ng/ml	No exposure calculations	No exposure calculations
	Schlumpf (2010)	Switzerland Women (n=54)	Human milk, Samples from 7-10 days, 30 days post	Propylparaben: Concentration in milk: 1.5 (1.88) ng/mL	Propylparaben: Infants from milk: **301.3 ng/kg bw/d**	Propylparaben: Infants from milk (max): **381.1 ng/kg bw day**

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
			partum.			
	Comments: The paraben concentrations of propyl- and butylparaben along with methyl- and ethylparabens, have been measured in several Danish studies of Danish children adult women/pregnant women. Exposure calculations have been performed for infants based on levels measured in milk. The measurements show that the detection of propyl- and butylparaben in the urine of Danish children and women are generally lower compared to the shorter chained parabens methyl- and ethylparaben. Further the measurements show that the highest exposure to parabens is among the youngest children and women.					
	References: *Frederiksen et al., (2014). Human urinary excretion of non-persistent environmental chemicals: an overview of Danish data collected between 2006 and 2012. Reproduction. 2014 Mar 4;147(4):555-65.* *Frederiksen et al., (2013b). Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. 2013 Nov;216(6):772-83.* *Schlumpf (2010). Exposure patterns of UV filters, fragrances, parabens, phthalates, organochlor, pesticides, PBDEs, and PCBs in human milk: Correlation of UV filters with use of cosmetics. Chemosphere 81 (2010) 1171–1183*					
Paracetamol						
Paracetamol	Nielsen 2015	Denmark: Children 6-11 years (n=144) Women (n=145)	Urine (morning spot)	Children, detected in all but 1 sample: 27 (8617) µg/L Mothers, detected in 100%: 120 (194,900) µg/L	No exposure calculations	No exposure calculations
	Comments: The urinary excretion of paracetamol have been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that paracetamol could be detected in nearly all samples. The concentration of paracetamol in the urine was not always dependent on the intake of paracetamol medication and the authors suggests other sources of paracetamol e.g. from the metabolism of the chemical aniline which is present in the diet.					
	References: *Nielsen JK, et al., (2015). N-acetyl-4-aminophenol (paracetamol) in urine samples of 6-11-year-old Danish school children and their mothers. Int J Hyg Environ Health. 2015 Jan;218(1):28-33.*					
PCB /TCDD						
PCB/TCDD	Meyer et al (2013)	Denmark: Adults, 138 exposed from building material and 151 non-exposed	Plasma	PCB 6 indicator (sum of PCB 28, 52, 101, 138, 153, 180) Non-exposed: 0.805 (2.508) µg/L Exposed: 2.715 (8.571) µg/L Dioxin-like PCBs (sum of 12): Non-exposed: 1.138 (3.402) µg/L	No exposure calculations	No exposure calculations

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
				Exposed: 4.700 (16.466) µg/L		
	Mørck et al (2014)	Denmark: Children 6-11 years (n=116) Women (n=143)	Plasma	Total PCB (PCB 152+138+180)*2 Children: 0.101 (0.628) µg/g lipid Mothers: 0.146 (0.692) µg/g lipid TCDD equivalents calculated with WHO toxic equivalence factors (TEF 2005) as ∑Dioxin-like PCB*TEF 2005: Children: 0.210 (0.920) pg TEQ/g lipid Mothers: 0.230 (1.030) pg TEQ/g lipid	No exposure calculations	No exposure calculations
	Lignell et al (2016)	Sweden: Women, 8-12 weeks postpartum (n=32)	Breast milk	Median (max): PCB 28: 0.85 (2.6) ng/g lipid weight PCB 153: 19 (67) ng/g lipid weight	Infant daily intake, mean ± SD: PCB 28: 5.4 ± 2.6 ng/kg bw/d PCB 153: 147 ± 74 ng/kg bw/d	Infant daily intake, maximum: PCB 28: 14 ng/kg bw/d PCB 153: 297 ng/kg bw/d
	Schlumpf et al. 2010	Human breast milk from Swiss mothers 2004-2006	Breast milk		PCB7 (sum of PCB PCB-28,-52,-101,-118, -138,-153,-180) **Median: 999 ng/kg/d**	PCB7 (sum of PCB PCB-28,-52,-101,-118, -138,-153,-180) **Max: 2733 ng/kg/d**
	Comments: The plasma concentrations of PCBs have been measured in Danish children and adults. Measurements have also been made on residents of known PCB contaminated buildings. Exposure calculations have been performed for infants based on the PCB concentrations measured in breast milk, which indicate quite high exposures. The measurements show that the Danish population is still exposed to PCBs even though their use have been banned for many years. Further, Meyer el al (2013) shows that indoor air may be an important source to PCB exposure, if living in buildings built with PCB-containing material.					
	References: *Lignell et al., (2016) Environmental organic pollutants in human milk before and after weight loss. Chemosphere 159 (2016) 96-102* *Meyer et al., (2013) Plasma polychlorinated biphenyls in residents of 91 PCB-contaminated and 108 non-contaminated dwellings—An exposure study International Journal of Hygiene and Environmental Health 216 (2013) 755– 762* *Mørck et al., (2014) PCB Concentrations and Dioxin-like Activity in Blood Samples from Danish School Children and Their Mothers living in Urbanand Rural Areas. Basic & Clinical Pharmacology & Toxicology, 2014, 115, 134–144* *Schlumpf M, Kypke K, Wittassek M, Angerer J, Mascher H, Mascher D, Vökt C, Birchler M, Lichtensteiger W. Exposure patterns of UV filters, fragrances, parabens,*					

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
	phthalates, organochlor pesticides, PBDEs, and PCBs in human milk: correlation of UV filters with use of cosmetics. Chemosphere. 2010 Nov;81(10):1171-83.					
Pesticides						
Pesticides - Dialkylphosphates (DAPs)	EPA (2015)	Denmark: Children 6-11 years (n=143) Women (n=145)	Urine (morning spot)	DMAP Children: 59.5 (318) nmol/L Mothers 50.7 (245) nmol/L DEAP Children: 37.8 (150) nmol/L Mothers 29.8 (135) nmol/L DAP Children: 106 (387) nmol/L Mothers 92.3 (386) nmol/L	No exposure calculations	No exposure calculations
	Comments: The urinary excretion of DAPs, with are metabolites of organophosphate pesticides such as Chlorpyrifos, have been measured in Danish school children and their mothers. Exposure calculations have not been performed, but the measurements show that the organophosphate metabolites could be detected in nearly all samples.					
	References: *PA (2016) Organophosphate metabolites in urine samples from Danish children and women.*					
PFAS (PFOA; PFOS; PFHxS)						
PFOA **PFOS** **PFHxS**	Bjerregaard-Olesen et al (2016)	Denmark, pregnant women, Aarhus Birth Cohort, 2008–2013 (n=1533)	Serum	Median (interquartile range) PFOA: 2.02 (1.53;2.64) ng/mL PFOS: 8.28 (6.02;10.8) ng/mL PFHxS: 0.48 (0.37;0.64) ng/mL	No exposure calculations	No exposure calculations
	Jensen (2015)	Denmark, pregnant women, Odense Birth Cohort, 2010–2012 (n=392)	Serum	PFOA: 1.58 (9.71); ng/mL PFOS: 8.10 (26.12) ng/mL PFHxS: 0.29 (7.28) ng/mL Higher concentrations of newer PFAS (PFDA and PFNA) was associated with miscarriage.	No exposure calculations	No exposure calculations
	Mørck (2015b)	Denmark: Children 6-11 years (n=116) Women (n=143)	Plasma	PFOA: Children : 3.02 (5.21) ng/mL Mothers: 1.59 3.38 ng/mL PFOS: Children : 8.63 (16.06) ng/mL Mothers: 7.57 (16.18) ng/mL	No exposure calculations	No exposure calculations

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
				PFHxS: Children : 0.34 (0.99) ng/mL Mothers: 1.59 (3.38) ng/mL		
	Vorkamp (2009)	Denmark Pregnant women, Odense child cohort (n=200)	Serum	Median (range) PFOA: 1.8 (0.31–9.7) ng/mL PFOS: 8.4 (3.1–26) ng/mL PFHxS: 0.22 (<LOQ–0.75) ng/mL	No exposure calculations	No exposure calculations
	Völkel (2008)	Germany, Women (n=70)	Breast milk	PFOA, only detected in 16% Range: 201-460 ng/L PFOS, median (range): 119 (28–309) ng/L	Infant of 5 kg bodyweight: 0.10 µg PFOS/day (using median) **= 0.02 µg/kg bw/d**	Infant of 5 kg bodyweight: 0.27 µg PFOS /day (using maximum value) = **0.054 µg/kg bw/d**
	Comments: The plasma concentrations of PFASs have been measured in several Danish studies of both pregnant women, non-pregnant women and children. Exposure calculations have not been performed from the serum/plasma levels, but the PFAS was detected in nearly all samples indicating widespread exposure. Based on the PFOS concentrations measured in breast milk in Germany an estimation of the daily exposure in infants was made. The levels are higher than the levels reported by EFSA, indicating higher exposure in breastfed infants. Jensen (2015) and Mørck (2015) show that women with show that women with more children have lower serum levels, which indicates that pregnancy and likely also breastfeeding status affects the PFAS levels in the blood.					
	References: *Bjerregaard-Olesen et al (2016) Time trends of perfluorinated alkyl acids in serum from Danish pregnant women 2008–2013. Environment International 91 (2016) 14–21* *Jensen et al (2015) Association between Perfluorinated Compound Exposure and Miscarriage in Danish Pregnant Women. PLoS ONE 10(4): e0123496.* *Mørck et al (2015b) PFAS concentrations in plasma samples from Danish school children and their mothers. Chemosphere 129 (2015) 203–209* *Vorkamp et al (2009). Polybrominated Diphenyl Ethers and Perfluoroalkyl Substances in Serum of Pregnant Women: Levels, Correlations, and Potential Health Implications. Arch Environ Contam Toxicol 67:9–20* *Völkel et al., (2008) Perfluorooctane sulphonate (PFOS) and perfluorooctanoic acid (PFOA) in human breast milk: Results of a pilot study. Int. J. Hyg. Environ.-Health 211 (2008) 440–446*					
Phthalates						
Phthalates	Bekö 2013	Denmark: Indoor air and dust measurements and total exposure (biomonitoring) in children 3-6 years (n=431)	Urine (morning spot) Dust samples in house and day cares	No urinary concentrations reported	Sum of indoor air contribution and other sources (calculated on biomonitoring data). The distribution of exposure is specified in table 5a: **DEHP: 4.77 µg/kg/d** **DBP: 3.56 µg/kg/d**	Sum of indoor air contribution and other sources (calculated on biomonitoring data). The distribution of exposure is specified in table 5a: **DEHP: 19.7 µg/kg/d** **DBP: 13.06 µg/kg/d**

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
					DIBP: 3.19 µg/kg/d **BBP: 0.49 µg/kg/d**	**DIBP: 16.06 µg/kg/d** **BBP: 2.90 µg/kg/d**
	Callesen 2014	Denmark: Children 3–5 years (n=440, 222 healthy controls, 68 clinically diagnosed with asthma, 76 with rhino conjunctivitis and 81 with atopic dermatitis)	Urine (morning spot)	Healthy controls, n = 222 **ng/mL** MEP: 16.0 (111.6) MnBP: 84.7 (256.8) MiBP: 74.2 (206.7) MBzP: 13.7 (71.4) MEHP: 5.2 (13.7) MEHHP: 33.5 (118.1) MEOHP: 19.2 (71.3) MECPP: 37.0 (135.8)	No exposure calculations	No exposure calculations
	Frederiksen 2014	Overview of several Danish studies in Denmark: Children and pregnant women	Urine (morning spot), 24 h urine samples	Median urinary concentrations: 10–100 ng/ml in spot urine Range: <LOD (<1 ng/ml) to several 1000-foldHigher. Highest amounts of DEHPm, followed by MiBP, MnBP, MEP, DiNPm, and MBzP was excreted.	No exposure calculations	No exposure calculations
	Frederiksen 2013	Denmark: Children 6-11 years (n=144) Women (n=145)	Urine (morning spot)	Median (95-perc) ng/mL DEP Children: 20 (68) Mothers: 29 (359) DiBP Children: 54 (193) Mothers: 36 (139) DnBP Children: 32 (99) Mothers: 20 (70) BBzP Children: 7 (31) Mothers: 4 (22)	µg/kg bw/d DEP Children: 0.53 **Mothers: 0.7-1.00** DiBP Children: 2.35-2.75 **Mothers: 1.6** DnBP Children: 0.7-0.856 **Mothers: 0.49-0.543** BBzP Children: 0.173-0.227 **Mothers: 0.094-0.131**	µg/kg bw/d DEP Children: 2.6-3.01 **Mothers: 3.6-10.5** DiBP Children: 7.55 **Mothers: 3.04-5.21** DnBP Children: 2.03-2.23 **Mothers: 0.996-1.34** BBzP Children: 1.1 **Mothers: 0.432-0.47**

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
				DEHP Children: 69 (236) Mothers: 40 (136) DiNP Children: 20 (111) Mothers: 13 (100	DEHP Children: 2.43-2.69 **Mothers: 1.56** DiNP Children: 1.1-1.2 **Mothers:0.6-0.8**	DEHP Children: 8.1-12.5 **Mothers: 4.37-5.12** DiNP Children:6.9-11.3 **Mothers: 3.4-5.5**
	Frederiksen 2011	Denmark: Children and adolescents 6–21 years (n=129)	One 24 h urine sample and two consecutive first morning urine samples.	MEP: 29 ng/mL MBzP: 17 ng/mL MBP(sum): 111 ng/mL DEHP: 107 ng/mL DiNP: 31 ng/mL,	µg/kg bw/d DEP: 1.09 BBzP: 0.62 DBP: 4.29 DEHP: 4.04 DiNP: 1.70	µg/kg bw/d DEP: 8.04 BBzP: 3.78 DBP: 11.3 DEHP: 10.7 DiNP: 5.78
	Fromme 2013	Germany, Toddlers 15-21 months (n=25)	Spot urine on 7 consecutive days resulting in 152 urine samples and samples of food and beverage (n=171)	No urinary concentrations reported	Daily total intake, Average 95-perc in µg/kg bw/d DEHP: 6.3 DBP: 3.6 DIBP: 5.3 BBP: 1.3 **DINP: 2.3** **DnOP: 0.04** **DPHP: 0.1**	Daily total intake, High 95-perc in µg/kg bw/d DEHP: 20.6 DBP: 1.24 DIBP: 11.1 BBP: 2.5 **DINP: 9.1** **DnOP: 0.35** **DPHP: 0.26**
	Boas 2010	Denmark: Children 4–9 years (n=845)	Urine (spot)	Median (max) ng/mL MEP Male: 21 (731) Female: 21 (684) MBP Male: 130 (6457) Female: 121 (1217) MBzP Male: 17 (4548) Female: 12 (272) MEHP Male: 4.5 (78) Female: 3.6 (231) MEHHP Male: 37 (1718) Female: 31 (1672)	No exposure calculations	No exposure calculations

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
				MEOHP Male: 19 (656) Female: 16 (734) MECPP Male: 30 (676) Female: 27 (1755)		
	Schlumpf (2010)	Switzerland Women (n=54)	Human milk, Samples from 7-10 days, 30 days post partum.	MEHP (DEHP): 26.2 (74.98) ng/g lipid in milk MnBP (DnBP): 5.95 (15.27) ng/g lipid in milk MiBP (DiBP) 24.25 (55.28) ng/g lipid in milk	Infant exposure from milk: Median: MEHP (DEHP): 5.158 µg/kg bw/d MnBP (DnBP) 1.079 µg/kg bw/d MiBP (DiBP) 3.508 µg/kg bw/d	Infant exposure from milk: Maximum: MEHP (DEHP): 20.381 µg/kg bw/d MnBP (DnBP) 4.978 µg/kg bw/d MiBP (DiBP) 9.999 µg/kg bw/d
	Comments: The urinary phthalate concentrations have been measured several Danish studies of Danish children adult women/pregnant women. Exposure calculations have been performed for both children and mothers. The calculated exposure estimations for children performed by Bekö et al (2013) was considered highly reliable representable for young child exposure and is taken forward in the analysis. The study is described in detail in appendix 5a. Furthermore the exposure calculations from Fromme et al (2013) on DINP, DnOP and DPHP, not covered by Bekö (2013) is taken forward as these are made on children in the relevant age group. For the majority of the phthalates the exposure seems higher in children compared to adults, except for MEP, which is a phthalate often found in cosmetics (Frederiksen 2013). The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population.					
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Siloxanes						

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
Siloxane D4	No relevant human biomonitoring studies were found.					
Triclosan						
Triclosan	Lassen 2016	Denmark, Pregnant women from the Odense Child Cohort (n = 514)	Urine (fasting morning spot)	0.88 (428) ng/mL	No exposure calculations	No exposure calculations
	Geens 2015	Belgium Overweight and obese (n = 151) and lean (n = 43) individuals	Urine	Obese: Median: 1.5 ng/mL 90-perc: 73 ng/mL Lean: Median: 0.9 ng/mL 90-perc: 5.1 ng/mL	Obese: **490 ng/kg bw/d**	Obese: **565 ng/kg bw/d**
	Frederiksen 2014	Overview of several Danish studies in Denmark: Children and pregnant women	Urine (morning spot), 24 h urine samples	Children: 1.45 (378) ng/mL Pregnant women: 0.82 (411) ng/mL	No exposure calculations	No exposure calculations
	Frederiksen 2013b	Denmark: Children 6-11 years (n=144) Women (n=145)	Urine (morning spot)	Children: 0.45 (271) ng/mL Mothers: 0.64 (581) ng/mL	No exposure calculations	No exposure calculations
	Comments: The urinary triclosan concentrations have been measured several Danish studies of Danish children adult women/pregnant women. Exposure calculations have not been performed on measurements from the Danish population, however, a study from Belgium estimated the exposure in obese adults. The biomonitoring measurements show that there are large differences in individual exposure with large ranges, in addition to an overall wide exposure in the general Danish population. The calculated exposure estimations, based on the urinary excretion of triclosan are lower than estimates based on the literature included in the present report.					
	References: *Geens et al. (2015). Daily intake of bisphenol A and triclosan and their association with anthropometric data, thyroid hormones and weight loss in overweight and obese individuals. Environ Int. 2015 Mar;76:98-105.* *Frederiksen et al., (2013a). Bisphenol A and other phenols in urine from Danish children and adolescents analyzed by isotope diluted TurboFlow-LC-MS/MS. Int J Hyg Environ Health. 2013 Nov;216(6):710-20.* *Frederiksen et al. (2014) Human urinary excretion of non-persistent environmental chemicals: an overview of Danish data collected between 2006 and 2012. Reproduction. 2014 Mar 4;147(4):555-65.* *Frederiksen et al (2013b). Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health.*					

Substance	Selected References	Country and target group(s)	Matrix	Measured concentrations Median (95-perc)	Exposure estimates Mean	Exposure estimates Max/95-perc.
	2013 Nov;216(6):772-83. *Lassen et al., (2016). Prenatal Triclosan Exposure and Anthropometric Measures including Anogenital Distance in Danish Infants. Environ Health Perspect. 2016 Feb 23.*					
UV filters						
Ethylhexyl Methoxycinnamate/ Octyl Methoxycinnamate (OMC) **Benzophenon 1 (BP-1)** **Benzophenone 2 (BP-2)** **Benzophenone 3 (BP-3)**	Frederiksen 2013a	Denmark: Children and adolescents (n=129)	Urine (24 h samples)	BP-3 All: 1.41 (37.1) ng/mL	BP-3: Children 6-10 years: **26.7 ng/kg bw/d**	BP-3: Children 6-10 years: **1388 ng/kg bw/d**
	Frederiksen 2013b	Denmark: Children 6-11 years (n=144) Women (n=145)	Urine (morning spot)	BP-3: Children: 1.8 (40) ng/mL Mothers: 3.7 (312) ng/mL	No exposure calculations	No exposure calculations
	Comments: Human biomonitoring of the UV-filter BP-3 have been performed in two Danish studies of Danish children, adult women and document wide exposure to this particular filter. Exposure calculations were performed for children 6-10 years of age (mean: 26.7 ng/kg bw/d, 1388 ng/kg bw/d 95p). The calculated exposures to BP-3 from the biomonitoring data are much lower compared to values presented by Danish EPA (see appendix 5b). The reason for this may be that the biomonitoring study was not performed on children using sunscreen, and therefore rather presents a background level.					
	References: *Frederiksen et al., (2013a). Bisphenol A and other phenols in urine from Danish children and adolescents analyzed by isotope diluted TurboFlow-LC-MS/MS. Int J Hyg Environ Health. 2013 Nov;216(6):710-20.* *Frederiksen et al (2013b). Urinary excretion of phthalate metabolites, phenols and parabens in rural and urban Danish mother-child pairs. Int J Hyg Environ Health. 2013 Nov;216(6):772-83.*					

Appendix 7a

Tables for establishing DNEL values for effects related to endocrine disruption

As the selection of data for derivation of DNELs for several compounds was carried out in previous projects (MST 2012) or was based on evaluations by EFSA or EU Risk assessment reports (EU RARs), the below tables refer to other reports for those compounds. For other compounds, data selection was carried out as part of the current project, and for those compounds, the below tables include more detailed descriptions of several studies for each compound. Principles for derivation of DNELs and an uncertainty regarding choice of method for risk assessment of endocrine disrupters are presented in Section 7. For each compound it is highlighted in **bold** which DNEL values are carried forward to cumulative risk assessment for anti-androgenic (aa), estrogenic (estro) or thyroid disrupting (thyr) effects. Abbreviations: AGD: anogenital distance; BMDL: benchmark dose low (in most cases derived from benchmark dose at 10% effect level); DNEL: derived no-effect level; LOAEL: lowest-observed adverse effect level; NOAEL: No-observed adverse effect level. For abbreviations of chemicals, see main abbreviation list.

Antioxidants/preservatives

BHA:							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL mg/kg bw/day**	**Assessment factor**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Hansen et al., 1982 cited in EFSA 2011	Pigs, young adult, dietary exposure 3 weeks before mating and 110 days into pregnancy to 0, 50, 200, 400 mg/kg bw/day of BHA	↑ abs and rel thyroid (and liver) weight at all tested dose levels	-/50/-	10x2x2.5x3= 150	333	333	No effect on endpoints sensitive to disturbance of sex hormones. Allometric scaling factor 2 for pigs
Jeong et al., 2005	Rats, two generation study, non-guideline, exposure pregestation, gestation and lactation and offspring exposed until 13 weeks of age, N=12, 0, 10, 100, 500 mg/kg bw/day of BHA	High dose: ↓ serum T4 in male F0 and female F1, altered thyroid histology in female F1. ↓ testosterone in male F0 and F1, ↓ weight of testis (abs) and ventral prostate (abs and rel) in F0 adults. Sperm parameters affected at all dose levels but most markedly at high dose. Middle dose: ↓ vaginal weight in adult F1.	Thyroid: 100/500/- AA: 10/100/-	100	Thyroid: 1000 AA: 100	**1000 ($DNEL_{thyr}$)** AA:100	EFSA Panel 2011 considered that effect sizes were too small or with too large variation and could not be used to derive a point of departure for risk assessment
Kang et al., 2005	Uterotrophic: Immature 20 day old	Uterotrophic: ↓ abs and rel uterus weight at	Uterotrophic: ND/50/-	300	166	166	No effect on thyroxine level or

	female rats, 3 days exposure to 50, 100, 250, 500 mg/kg bw/day of BHA. Hershberger: 51-day old castrated male rats, 10 days exposure to 50, 100, 250, 500 mg/kg bw/day of BHA without TP coadministration or to 250 mg/kg bw/day with TP coadministration.	all doses; no effect on epithelial cell height. Also ↓ abs and rel uterus weight when supplemented with ethinyl estradiol. Hershberger: no effect of BHA on weights of androgen-sensitive organs when administered alone, but BHA increased ventral prostate weight when coadministered with testosterone propionate (TP).	(anti-estrogenic effect) Hershberger: no sign of antiandrogenic or androgenic effect				thyroid weight after 10 days in Hershberger study.
Zhu et al., 1997	Female CD1 mice, uterotrophic assay, 18 days dietary exposure to 0.75% BHA before administration of estradiol or estrone ()	BHA exposure inhibited the uterotrophic effect of estradiol or estrone and lowered serum estradiol and estrone levels compared to controls.	One dose only; 0.75% in diet		ND	ND	One dose only; not clear what 0.75% in diet corresponds to in mg/kg bw/day
Comments: **$DNEL_{thyr}$ of 1000 µg/kg bw/d** derived from reproductive toxicity study by Jeong et al., 2005, was selected for cumulative risk assessment because the observed effects were observed following a relevant exposure period for the current project and the thyroid disrupting effect of BHA was confirmed in a pig study. No DNEL for antiandrogenic or estrogenic effect was set, as the pattern of effects of BHA show mixed endocrine disrupting effects, but not with a clear anti-androgenic or estrogenic mode of action. Reduced vaginal weight in female offspring and adverse effects on sperm motility and sperm count were seen in a study by Jeong et al., 2005, but a study by Kang et al., 2005, indicated no anti-androgenic effects in a Hershberger assay, but clear anti-estrogenic effects in a uterotrophic assay. In contrast, in vitro studies indicated anti-androgenic and estrogenic effects (see EFSA 2011 for references). In a report by EFSA 2011, the study by Jeong et al., 2005, was not considered relevant for risk assessment, but in an evaluation by (MST/DTU 2012) the overall weight of evidence was considered sufficient for evaluation of BHA as an endocrine disrupter.							
BHT							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL mg/kg bw/day**	**Assessment factor**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Olsen et al., 1986	Wistar rats, 13 weeks premating, exposure of offspring until 144 weeks of age, 0, 25, 108, 276 mg/kg bw/day in diet, N=40-60	Reduced thyroid follicular size, reduced colloid, and ↑ number of follicular cells at mid and high dose. No change in serum thyroxine	25/108/-	100	250 (oral)	**250 ($DNEL_{thyr}$)**	Described as thyroid hyper-activity, not hypo-activity, but considered to be part of the same effect pattern as other thyroid disrupting

							compounds
Søndergaard and Olsen 1982	Rats, 28 days, 0, 25, 250 mg/kg bw/day in diet.	↑ number of follicle cells at high dose. No change in T3 or T4. Increased uptake of iodine	25/250/-	100	250	**250 ($DNEL_{thyr}$)**	JECFA 1996 used NOAEL to set ADI
Comments: **DNELthyr of 250 µg/kg bw/d** was derived from two rat studies by Olsen et al., 1986 and Søndergaard and Olsen, 1982. This evaluation is based on detailed data selection in a report by EFSA 2012 applying these data to set an ADI. According to EFSA 2012, possible behavioral effects have been seen in offspring and For details, please refer to that report. According to SIN list (2014), in vitro studies indicate ability of endocrine disruption of sex hormones, but this has not been addressed in the current project.							
Triclosan							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Stoker et al 2010	Rats	Significantly earlier age of onset of vaginal opening in pubertal assay.	75/150/-	2.5*4*10=100	750	**750 ($DNEL_{estro}$)**	↑ uterine weight in uterotrophic assay in intact immature animals receiving triclosan and EE, compared to EE-treated alone at 4.69–37.5 mg/kg bw/day (same paper). This indicates effect at lower dose level, but in an unrealistic model assay (compared to immature rats not exposed to EE).
(Zorilla et al., 2009)	Wistar rats	↓ T4 after 31 days dosing of young male rats	3/30/-	2.5*4*10=100	30	**30 ($DNEL_{thyr}$)**	Wistar rats, perhaps more sensitive to triclosan than LE rats.
Comments: **$DNEL_{thyr}$ of 30 µg/kg bw/d** was derived from a study in rats (Zorilla et al., 2009). **$DNEL_{estro}$ of 750 µg/kg bw/d** was derived from a study in rats Stoker et al., 2010). The data for Triclosan showing thyroid disrupting effects is considered to be robust. Triclosan modulates estrogen metabolism rather than binding to/activating the estrogen receptor. Regarding the estrogenic effect, data for DNEL derivation is considered less robust, but the estrogenic mode of action of triclosan is corroborated by results showing increased uterine weight in an uterotrophic assay (Stoker et al., 2010). The evaluation of thyroid disrupting effect is based on detailed data selection in a report by MST 2012 (pregnant consumers).							

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Brominated compounds

TBBPA							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2011a (based on van der Ven et al., 2008)	28-day study and 1-generation study in Wistar rats. Mixed in feed.	Changes in thyroid hormone levels (↓ T4), see below	-/-/16	100 (additional factor considered necessary, but not specified in report)	160	**160 ($DNEL_{thyr}$)**	CONTAM Panel noted that an additional factor would be needed to cover deficiencies in the database – not specified in report due to large margins of exposure.
MST 2012 (based on van der Ven et al., 2008)	28-day study and 1-generation study in Wistar rats. Mixed in feed.	At highest doses: ↓ T4 in both studies, no effect on thyroid weight or histology. At lower doses (but not high): ↑ absolute weight of testes and pituitary in male rat (BMDL10 of	30/100/-	2.5*4*10=100	300	300	In MST 2010 NOAEL and LOAEL were determined from data in the van der Ven paper, although the authors only showed BMD. Also ↑ testes and pituitary size, but nothing on female reproduction. Effects on testes weights were not

		0.5 mg/kg bw/day)					used for risk assessment in EFSA 2011 due to lack of effect in other studies and unusual dose-response curves. In the current project these data are considered insufficient to see a DNELaa or DNELestro for TBBPA.

Comments: **$DNEL_{thyr}$ of 160 µg/kg bw/d** was derived from two studies in pregnant and non-pregnant rats (van der Ven et al., 2008). In contrast to the evaluation by MST 2012, the DNEL based on BMDL derivation was selected for risk assessment in the current project. Data for TBBPA, showing thyroid disrupting effects is considered to be robust, but the determination of DNEL is considered to be less robust, i.e. subject to some uncertainty. These evaluations are based on detailed data selection by EFSA 2011a and MST 2012 (pregnant consumers).

HBCDD

Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
(Van der ven et al 2006)	Rats, 28 day study, oral, 7 doses from 0.3 to 200	↑ thyroid weight and histological changes (NOAEL 10 mg/kg bw/day), ↓ T4 (NOAEL 30 mg/kg bw/day), BMDL of 22.9 mg/kg bw/day is considered relevant for thyroid in the EU RAR.	-/-/22.9	40 (EU RAR 2008 explains this as 10 for intraspecies differences, 4 for rat-to-human differences, but no factor for subchronic to chronic exposure)	573	573	Conclusions based on EU RAR 2008. EFSA 2011b evaluated the same data, but instead used BMDL for neurodevelopmental effects for risk assessment.
Adjusted data from (Van der ven et al 2006)	Rats, 28 day study, oral, 7 doses from 0.3 to 200	↑ thyroid weight and histological changes (NOAEL 10 mg/kg bw/day), ↓ T4 (NOAEL 30	-/-/0.38 (based on calculations of body burdens by methods in EFSA 2011b)	2.5 (inter-species differences in dynamics) * 3.2 (individual differences in kinetics) =8 (EFSA 2011b)	48	**41** (absorbed fraction 0.85 according to EFSA 2011b) **(DNELthyr)**	A one compartment model was used for accumulation in adipose tissue. Chronic human intake = body burden (mg/kg) *

		mg/kg bw/day), BMDL of 22.9 mg/kg bw/day is considered relevant for thyroid in the EU RAR.					ln2/t½ As a 'worst-case' the longest human half-life identified for HBCDDs of 219 days was used. For rat adipose tissue a half- life of 3.6 days was used
Comments: **$DNEL_{thyr}$ of 41 µg/kg bw/d** was derived from a 28-day study in rats based on conclusions in EU Risk Assessment report 2008 and recalculated to take account for accumulation using body burden calculations as described in EFSA 2011. Reproductive effects (reduced ovarian follicle reserves) were observed in a two-generation reproductive toxicity study, and anti-androgenic and anti-estrogenic effects were observed in vitro, but no DNEL could be derived based on these data as presented in the EU RAR (2008).							
Deca-BDE **CAS 1163-19-5**							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2011c (based on Rice et al., 2007)	Mice, PND 2-15, oral. 0, 6, 20 mg/kg bw/day	Dose dependent decrease of T4 in males on PND21	-/6/6.8	2.5 from BMDL10 (EFSA 2011)	2.7	**2.7 ($DNEL_{thyr}$)**	EFSA notes that studies showing thyroid effects with repeated administration would result in considerably higher body burdens, i.e. this is a conservative approach. The observed effects on thyroid hormone levels were not always consistent, but considered human relevant. In mice: NOAELs generally 10-20 mg/kg bw/day. Conclusion on reproductive toxicity: given during gestation and/or postnatally, generally no reproductive or developmental effects were seen at doses up to 500 mg/kg b.w. per day.
EU RAR 2002							EU RAR concluded that endocrine disruption by interference with thyroid hormone system is not relevant, as mild effects (follicular cell hyperplasia)

							were seen with lifetime exposure and no effects in two species were seen with 13 weeks treatment
Background document for RAC/SEAC opinion 2015	Table on several rat studies; in utero, postnatal or subchronic exposure						An overall evaluation of several listed studies showed high variability, but several studies showed effects on thyroid hormones at approximately 100 mg/kg bw/day. No data selection/ DNEL determination for thyroid effects.
Tseng et al 2013	Pregnant rats, GD 0 to GD 17, exposed by gavage to 0, 10, 500 or 1500 mg/kg bw/day of Deca-BDE	Sperm effects (DNA damage) at all doses; at high dose also abnormal sperm heads and ↓ male AGD and AGDi	High: 500/1500/- Low: -/10/-	100 (from NOAEL) 300 (from LOAEL)	High: 5000 Low: 33	High: 5000 Low: 33	Some uncertainty whether sperm DNA effects are due to antiandrogenic effect.
van der Ven et al., 2008	Rats, 28 day study, oral 0–1.87–3.75–7.5–15–30 mg/kg bw/day	↑ seminal vesicle weight. Indications of ↓ epididymis weight, but no BMDL determined. No effect on sperm count or morphology	-/-/0.2	100	2	2	. BMDL approach, no NOAELs listed. EFSA noted a large degree of variability of these data and lack of clear dose-response relationship.
Comments: **$DNEL_{thyr}$ of 2.7 µg/kg bw/d** was based on a data selection in EFSA 2011. No DNEL has been set for anti-androgenic or estrogenic effects as it is not clear whether effects on male reproductive organs (seen in studies by Tseng et al., 2013 and van der Ven et al., 2008) are related to an endocrine mode of action. According to EFSA 2011, the elimination half-life of BDE-209 does not differ by orders of magnitude between animals and humans, and the animal BMDL10 expressed as an external dose can be compared with the estimated human dietary exposure.							

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Chlorinated compounds

Dioxins and dioxin-like PCBs							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
(Faqi et al., 1998)	One dose of PCB 77 at GD 15, Wistar rats	↓ AGD, ↑ weight of testis and epididymis, ↓ relative seminal vesicle weight, ↓ serum testosterone, altered pup body weight	(for calculation of body burden and conversion to human equivalent doses, see EC-SCF 2001)		2E-06	**2E-06 (DNELaa, food and indoor air)**	DNEL is in TEQ (toxic equivalency quotient; i.e. dioxin-equivalents) 2 pg TEQ/kg/day corresponds to TDI cf EU (Scientific Committee for Food and FAO/WHO (EC-SCF 2001). Conversion to body burden has been

							taken into account.
(Sewall et al., 1995)	?	Changed thyroid histology, ↓ T4, ↑ TSH .	?		6E-06	**6E-06 (DNELthyroid, food and indoor air)**	DNEL is in TEQ, see comments. Conversion to body burden has been taken into account.
Comments: **$DNEL_{aa}$ of 2 pg TEQ/kg bw/d** for food and indoor air corresponds to the TDI (or rather: TWI, tolerable weekly intake, of 14 pg TEQ/kg bw/d) set by Scientific committee for food (2001). D**NEL_{aa} of 3 ng PCBtotal/kg bw/d** for dust was based on reproductive effects in monkeys (Arnold et al., 1985). **$DNEL_{thyr}$ of 6 pg TEQ/kg bw/d** for food and indoor air was based on the fact that in order to observe thyroid effects (Sewall et al., 1995), an animal must be exposed to TCDD body burdens which are 3 times higher than the body burdens causing reproductive adverse effects (see MST 2012). Data for Dioxins and dioxin-like PCBs showing antiandrogenic and thyroid disrupting effects are considered robust. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers). Separate values for food and indoor environment were included because of differences in composition of PCB congeners in food and indoor air/dust. In food, selected dioxin-like PCB congeners are measured and calculation of toxic equivalency factors for each congener is applied for determination of a toxic equivalency quotient (TEQ) for the group of PCBs. This TEQ is compared with the DNELs of 2 or 6 pg TEQ/kg bw/d. For indoor environment, data are not available to calculate specific TEQs, and therefore separate DNELs for total PCB are applied as described below.							
PCBs, total							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Sundhedsstyrelsen 2013; WHO/IPCS 2003 (based on Arnold et al., 1995; see below)	Rhesus monkey, see below	Immunological effects in offspring and impaired fertility of dams.	-/0,005/-	300= 10 (intraspecies)*3 (interspecies) * 10 (LOAEL to NOAEL) =300	0.02 (total PCB)	0,02 (total PCB)	TDI for mixtures of PCBs with similarities to Aroclor mixtures. This value is not in TEQs but adequate for comparison with measures of total PCB or selected marker-PCBs. As this TDI is based on immunological effect, it may be an overestimation of risk of endocrine disruption of reproductive system.
(Arnold et al., 1995)	Rhesus monkeys,daily dosing with a commercial PCB mixture Aroclor 1254 capsule; 0, 5, 20, 40, 80 µg/kg	Impaired fertility of dams	-/0,005/-	150= 10 (intraspecies)*5 (interspecies) *3 (LOAEL to NOAEL)	0.033	**0.033 (DNELaa, dust)**	Conversion to body burden has been taken into account (steady state reached in dam

	bw/d. Dams were dosed from at least 37 months before mating to week 7 after birth and again from 22 weeks after birth and continuing to until 66 months of total exposure,n=16						before mating). A smaller LOAEL-to-NOAEL assessment factor is applied than in Sundhedsstyrelsen 2013, see Table 7.1 for assessment factors used in the current project.
Comments: Separate values for food and indoor environment were included because of differences in composition of PCB congeners in food and indoor air/dust. For indoor environment, data are not available to calculate specific TEQs. However, the composition of dioxin-like PCBs is considered to be comparable to Aroclor mixtures, and therefore the $DNEL_{aa}$ for indoor environment is based on a study on an Aroclor mixture. The observed effects were on dam fertility and may be related to endocrine disruption as seen for some PCB congeners (estrogenic, anti-estrogenic of anti-androgenic mode of action), but as little is known on effects onhe offspring reproductive system, some uncertainty is associated with this DNEL for indoor environment. No $DNEL_{thyr}$ could be calculated for dioxin-like PCBs in dust, and the contribution of dioxin-like PCBs in dust will not be included in the cumulative risk assessment of thyroid disrupting chemicals, and this may lead to an underestimation of cumulative risk.							

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Fluorinated compounds

PFOA							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**

			(mg/kg bw/day)				
(Butenhoff et al., 2002)	Monkeys, diet, 0, 3, 10, or 30 (decreased to 20) mg/kg/day for 26 weeks	↓ T4 and ↑ TSH at 26 weeks; T3 reduction at high dose	-/3/-	2.5*2*10*3=150	20	**20 (DNELthyr)**	Effect is also observed after just 5 weeks of dosing at 10 mg/kg. Discrepancy between data in US EPA 2016 and published paper. The US EPA 2016a document did not include human equivalent dose (HED) calculations on monkey data, and therefore this figure does not take differences in rats and humans regarding accumulation/body burden into account.
(Butenhoff et al., 2004)	Rats, 2-generation study, diet, 0, 1, 3, 10, and 30 mg/kg/day	Delayed puberty, male and female rats	10/30/- (human equivalent dose: 0.064/0,192/-)	2.5*4*10=100 (from human equivalent dose: 3*10=30)	100	100 (based on human equivalent dose calculation: 2.1) (not considered robust enough to include as DNELaa for PFOA)	To take account for differences in rats and humans regarding accumulation/body burden, human equivalent doses (HED) were calculated. See US EPA 2016a for further description. A 100 times lower RfD of 0.02 µg/kg bw/d was set by US EPA using data on kidney weight in the same study.
Comments: **$DNEL_{thyr}$ of 20 µg/kg bw/d** was derived from a chronic toxicity study in monkeys (Butenhoff et al., 2002). Data for thyroid disrupting effects are in animal models are less robust, but strengthened by support from human studies. Data showing anti-androgenic effects are not considered robust enough to apply the suggested DNEL aa further in the current project. According to US EPA 2016: "*The dose-response relationship of serum total T4 with PFOA exposure has yet to be fully evaluated and the lowest effective dose remains unknown*". These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers), and adjusted by HED calculation methods presented by US EPA 2016.							
PFOS							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Zhao et al., 2014	Rats, gavage GD 11-	↓ testosterone,	-/5/-	3*2.5*4*10=300	17	17	To take account for

	19	and ↓ expression of genes related to steroid synthesis at GD 21. Effect on gene expression from 5 mg/kg bw/d.	(human equivalent dose: -/0.007/-)	(from human equivalent dose: 3 (LOAEL to NOAEL)*3 (interspecies toxicodynamic) *10(intraspecies)=90)		(based on human equivalent dose calculation: **0.08**) **(DNELaa)**	differences in rats and humans regarding accumulation/body burden human equivalent doses (HED) were calculated. See US EPA 2016b for further description of HED determination. Comparable effects on hormone production in adult rats (Lopez-Doval et al., 2015; Wan et al., 2011).
EFSA 2008 (based on Seacat et al.,2002)	Monkeys, 183 days	↓ T3 and T4, ↑ TSH	0.03/0.15/-	200 jf EFSA 2008	0.15	0.15	NOAEL of 0.03 in EFSA 2008 to set TDI of 150 ng/kg
US EPA 2016b (based on Seacat et al.,2002)	Monkeys, 183 days	↓ T3 and T4, ↑ TSH	0.15/0.75/- Human equivalent doses: 0.0031/0.013/-	3 (interspecies toxicodynamic) * 10 (intraspecies)=30	- (not relevant)	**0.1 (DNELthyr)**	Human equivalent dose, i.e. internal dose corrected for species differences in toxicokinetics. Uses a higher NOAEL than EFSA 2008.
Comments: **$DNEL_{aa}$ of 0.8 µg/kg bw/d** was derived from a study in pregnant rats (Zhao et al., 2014) and supported by similar findings in other studies. **$DNEL_{thyr}$ of 0.1 µg/kg bw/d** was derived from a study in monkeys and calculated using a method described by US EPA 2016b. Data for PFOS, showing thyroid disrupting effect is considered robust, but data for anti-androgenic effects are considered less robust. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers), but updated with recent data and adjusted by HED calculation methods presented by US EPA 2016b.							
PFHxS							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Ramhøj et al., 2015	Rats, gavage GD 7 to PND 17	↓ T3 and T4 in pups PND 16/17 and ↓ T4 in dams GD 15	0.05/5/-	300 from LOAEL	17	**17 (DNELthyr)**	Published abstract. Large dose span and therefore DNEL selection is based on LOAEL.
Comments: **$DNEL_{thyr}$ of 17 µg/kg bw/d** was derived from a study on perinatal exposure of rats. Data showing thyroid disrupting effect is considered robust, but DNEL calculation is not currently adjusted for differences in rats and humans regarding accumulation/body burden.							

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Phthalates

DEHP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Wolfe and Layton 2003; Christiansen et al. 2010	Rats, combined results of two reproductive toxicity studies, oral	↓ male AGD, ↑ male nipple retention, reproductive toxicity (germ cell depletion, ↓ testis weight) in offspring	5/10/-	2.5*4*10 = 100	50 (oral)	**35** (oral absorption of 70%; ECHA/RAC 2012) **($DNEL_{aa}$)**	Two studies were used to set NOAEL (Wolfe and Layton 2003) and LOAEL (Christiansen et al., 2010). NOAEL applied in EU RAR 2008 and ECHA/RAC 2012
Poon et al. 1997	Rats, 13-week study, oral	Altered thyroid histology	37.6/375.2/-	2.5*4*10 = 100	376	**263** (oral absorption of 70%; ECHA/RAC 2012) **($DNEL_{thyr}$)**	
Comments: **$DNEL_{aa}$ of 35 µg/kg bw/d** was derived from two reproductive toxicity studies. **$DNEL_{thyr}$ of 376 (188) µg/kg bw/d** was derived from a 13-week study in rats. These evaluations are considered robust and are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
DBP							

Reference	Study design (and exposure route)	Effect-parameter	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELeksternal µg/kg bw/d	DNELinternal µg/kg bw/d	Notes
Lee et al., 2004	Pregnant rats, GD 15 to 21. 0, 20, 200, 2000, 10000 mg/kg feed corresponding to 0, 2, 20, 200, 1000 mg/kg bw/day.	Alterations in male and female breast tissue, histological alterations in testis of offspring	ND/2/-	3*2.5*4*10 = 300 (ECHA/RAC 2012)	6.7	**6.7** (oral absorption of 100%; ECHA/RAC 2012) **($DNEL_{aa}$)**	EFSA 2005a, ECHA/RAC 2012
Comments: **$DNEL_{aa}$ of 6.7 µg/kg bw/d** was derived from a developmental toxicity study by Lee et al., 2004; data also applied by EFSA (2005) and ECHA/RAC 2012. Data for DBP showing antiandrogenic effects are considered robust and in agreement with several other studies showing antiandrogenic effects of DBP. The applied NOAEL is somewhat lower than NOAEL for reduction of testosterone in rat fetuses or reduced AGD in males. This evaluation is based on detailed data selection in a report by MST 2012 (pregnant consumers).							
DiBP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Rea-across fra DBP jf ECHA 2016	See DBP	See DBP	-/2.5/-	3*2.5*4*10 = 300	8.3	**8.3** (oral absorption of 100%; ECHA/RAC 2012) **($DNEL_{aa}$)**	Read-across from DBP, see ECHA 2016
Saillenfait et al., 2008	Rats GD 12-21, gavage 0, 125, 250, 500, 625 mg/kg bw/day	↓ AGD, ↑ nipple retention in male offspring	-/125/-	3*2.5*4*10 = 300	417	417	
Comments: **$DNEL_{aa}$ of 8.3 µg/kg bw/d** was derived by read-across from DBP as proposed in restriction dossier by ECHA 2016. Data for DiBP showing antiandrogenic effects are considered robust and supported by a study in perinatally exposed rats (Saillenfait et al., 2008) and in agreement with other studies showing similar effects (see ECHA 2016). These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
BBP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Tyl et al., 2004	Rats, two-generation study, 0, 20, 100, 500 mg/kg bw/day.	↓ AGD in male offspring	50/250/-	2.5*4*10 = 100	500	500 (oral absorption of 100%; ECHA/RAC 2012) **($DNEL_{aa}$)**	EFSA 2005b, ECHA/RAC 2012
Comments: **$DNEL_{aa}$ of 500 µg/kg bw/d** was derived from a two-generation study showing reduced AGD in male offspring (Tyl et al., 2004). Data for BBP showing antiandrogenic effects are considered robust and in agreement with other studies showing similar effects. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers) and ECHA/RAC 2012.							
DPP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Hannas et al.,2011	Pregnant rats,	↓ AGD PND2, ↓	33/100/-	2.5*4*10 = 100	330	**330**	

	gavage GD 8 to 18	expression of steroid genes in testes of fetuses. ↑ Nipple retention at next dose level				**(DNEL$_{aa}$)**	
Comments: **DNEL$_{aa}$ of 330 µg/kg bw/d** was derived from an in utero study showing antiandrogenic effects. Data for DPP showing antiandrogenic effects are considered robust. Older studies show impaired fertility in mice at high doses, but no reproductive toxicity studies on lower doses of DBP have been found. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
DnHP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Saillenfait et al.,2009	Rats	↓ male AGD, increase in frequency of malformations	50/125/-	2.5*4*10 = 100	500	**500 (DNEL$_{aa}$)**	↑ nipple retention, delayed sexual maturation, ↓ weight of reproductive organs at ≥ 250
Hinton et al.,1986	Rats 3, 10, and 21 days	Histological changes in thyroid indicating hyperactivity	ND/1824/-	2.5*4*10*3 = 300	6100	**6100 (DNEL$_{thyr}$)**	Noted as ”sufficient data” to show thyroid disrupting effect according to NTP monograph (NTP CERHR 2003a)
Comments: **DNEL$_{aa}$ of 500 µg/kg bw/d** was derived from a study in perinatally exposed rats (Saillenfait et al., 2009). **DNEL$_{thyr}$ of 6100 µg/kg bw/d** was derived from a study in rats following short-term exposure. Data for DnHP, showing antiandrogenic and thyroid disrupting effects are considered reliable, but the DNEL derivation for thyroid disrupting effect is considered less robust due to use of high doses and short term exposure. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
DnOP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Poon et al.,1997	Rats	Thyroid histological effects in 13 weeks study in rats	36.8/350/-	2.5*4*10 = 100	368	**368 (DNEL$_{aa}$)**	Cited in ECHA review (ECHA 2010) and NTP monograph (NTP CERHR 2003b). Thyroid effects also observed in 21 days study at higher doses
Comments: **DNEL$_{aa}$ of 368 µg/kg bw/d** was derived from a 13 week study in rats (Poon et al., 1997). Data for DnOP showing thyroid disrupting effects are considered robust. No data for effects on the reproductive system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							

DiNP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Boberg et al., 2011	Pregnant rats, oral exposure GD 7 to PND 17, 0, 300, 600, 750, 900 mg/kg bw/day	↑ nipple retention in males. ↓ sperm motility and AGD at higher doses	300/600/-	2.5*4*10 = 100	3000	**1500 ($DNEL_{aa}$)**	50% oral absorption; ECHA 2013
Comments: **$DNEL_{aa}$ of 1500 µg/kg bw/d** was derived from a study in perinatally exposed rats (Boberg et al., 2011) and supported by other studies showing similar effects. Data for DiNP showing antiandrogenic effects are considered robust. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
DPHP							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Bhat et al., 2014, with reference to study by BASF AG (2009)	Two-generation study in rats, supported by a 13-week study in rats.	Thyroid hypertrophy/ hyperplasia at BMDL10 of 10 mg/kg bw/day	-/-/10	100	100	**100 ($DNEL_{aa}$)**	Data from BASF 2009 not available, but applied for DNEL derivation in paper by Bhat et al., 2014.
Comments: **$DNEL_{thyr}$ of 100 µg/kg bw/d** was derived from a two generation study in rats and supported by a 13-week study in rats (Bhat et al., 2014).							

DCHP:							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL mg/kg bw/day**	**Assessment factor**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Li et al., 2016	Rats, gavage, GD 12 to 21 0, 10, 100, 500 mg/kg bw/day	↓ absolute male AGD and reduction of testicular testosterone production from 100 mg/kg. Histological changes in testes ↓ expression of steroidogenesis related genes at all doses	10/100/-	100	100		NOAEL for AGD and testosterone reduction is used for DNEL determination
Hoshino et al., 2005	DCHP 99.9% purity, two generation study (diet), n=24, SD rats. 0, 240, 1200, 6000 ppm corresponding to 0, 18, 90, 457 mg/kg bw/day	↑ thyroid weight at high dose in F0, thyroid follicular cell hypertrophy (slight) in F0 and F1. ↓ abs and relative prostate weight at high dose in F1, severe seminiferous tubule atrophy in high dose. Possibly delayed puberty in F1 males. ↓ abs and relative AGD and ↑ nipple retention in males at high dose in F1 and F2 and at intermediate	AA: 18/90/- (240/1200/- ppm) Thyroid: 90/457/-	100	AA: 180 Thyroid: 900	**180 ($DNEL_{aa}$)** **900 ($DNEL_{thyr}$)**	

		dose in F2.					
Saillenfait et al., 2009	Rats, gavage, GD 6 to GD 20, 0, 250, 500, 750 mg/kg bw/day	↓ relative AGD in males at all dose levels	-/250/-	300	833		
Yamasaki et al., 2009	Rats, gavage GD 6 to PND 20, 0, 20, 100, 500 mg/kg bw/day	↓ male anogential distance and nipple retention at 500 mg/kg bw/day. Hypospadias and small testes in a few high dose males. ↓ weight of male reproductive organs in adult males and histological changes in testes	100/500/-	100	1000		Effect size at lower doses not well described
Aydogan Ahbab & Barlas, 2013	Rats, gavage, GD 6 to GD 19, 0, 20, 100, 500 mg/kg bw/day	↓ abs and rel testis weight at high dose, ↑ percentage of abnormal sperm at all dose levels (same magnitude at all doses). Histological changes in testes at all doses	?				Relevance of histological findings not clear. AGD not assessed
Comments: **$DNEL_{aa}$ of 180 µg/kg bw/d** derived from two generation study by Hoshino et al., 2005The studies by Li et al., 2016 and Hoshino et al., 2005, both showed anti-androgenic effects at 90-100 mg/kg bw/d. The highest NOAEL of the two studies was 18 mg/kg bw/d (Hoshino et al., 2005). These findings were supported by findings by Saillenfait et al., 2009 and Yamasaki et al., 2009, at higher doses. The study by Aydogan Ahbab and Barlas, 2013, was considered less appropriate because of poor reporting. Descriptions are based on RAC 2015. According to RAC 2015 DCHP or metabolite MCHP induced estrogenic activity in some but not all in vitro studies, whereas no estrogenic effects were seen in uterotrophic assays in rats. Overall, these findings are considered to be related to a steroid synthesis inhibiting mode of action and DCHP can thus be grouped with anti-androgenic chemicals in this project. **$DNEL_{thyr}$ of 900 µg/kg bw/d** derived from two generation study by Hoshino et al., 2005, was selected for cumulative risk assessment of thyroid disrupting effects.							

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Medicine

Paracetamol							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Holm et al., 2016	Mice, gavage GD 7 to GD 20. 0, 50, 150 mg/kg bw/day of paracetamol (or corresponding doses of aniline). n=10	↓ AGD in 10 weeks old male offspring	50/150/-	100	500	500	

	litters. Examination of AGD in pups at age 4, 6, 8 and 10 weeks.						
Kristensen et al., 2011	Rats, gavage GD 13 to PND 21. 0, 150, 250, 350 mg/kg bw/day of paracetamol. n=4-5 litters in first study, n=6 litters in second study.	↓ AGDi in male fetuses at GD 21 at all doses	-/150/-	300	500	**500 (DNELaa)**	
Comments: DNELaa of 500 µg/kg bw/d was derived from a study in prenatally exposed rats (Kristensen et al., 2011) and supported by a study in mice (Holm et al., 2016) showing reduced male AGD at birth and at 10 weeks of age, respectively. In addition to these signs of antiandrogenic effect in rats, epidemiological studies from Denmark and other European countries have shown associations between paracetamol intake in early pregnancy and increased risk of cryptorchidism (Jensen et al 2010; Snijder et al 2012). Other studies have found associations between maternal paracetamol intake and other painkillers and short anogenital distance in sons (Lind et al., 2016; Fisher et al 2016). These findings point to a possible antiandrogenic effect of paracetamol also in humans, but other studies find no such associations, and no associations with presence of hypospadias have been seen.							

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Parabens

Butyl- and propylparaben							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
SCCS 2011, SCCS 2013 (Fischer et al., 1999; Kang et al., 2002; Oishi 2002; Lemini et al., 2003; Lemini et al., 2004)	Rats, several studies on perinatal exposure to butylparaben.	↓ semen quality at exposure of young and pregnant rats	2/10/-	2.5*4*10=100	20	**20** (not adjusted for oral absorption fraction in study on oral dosing) **($DNEL_{estro}$)**	SCCS uses the same NOEL for propyl- and butylparaben. Overall assessment of several studies considered by SCCS 2011 and 2013.
(Boberg et al., 2016)	Rats	↓ semen quality at exposure of young and pregnant rats	-/10/-	3*2.5*4*10=100	33		

Comments: **$DNEL_{estro}$ of 20 µg/kg bw/d** was derived from a study on butylparaben showing absence of reproductive effects in rat offspring at 2 mg/kg bw/day, and an estrogenic mode of action supported by increased uterine weight in uterotrophic studies (as evaluated by SCCS 2013). Data for Butylparaben, showing endocrine disruptive (estrogenic) effects is considered to be reliable. Data for Propylparaben, showing endocrine disruptive (estrogenic) effects is considered to be reliable, but the determination of DNEL is considered to be less robust, i.e. subject to some uncertainty**.** Considering the recent findings of reduced sperm count at doses from 10 mg/kg bw/day, the determination of DNEL is considered to be robust**.** No data for effects on the thyroid hormone system was located.

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Phenols

Bisphenol A							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Comments**
EFSA (Based on Tyl et al. 2008)	Rat, two-generation study	Extrapolation from BMDL for kidney effects to cover also reproductive effects (e.g. mammary gland effects and ↓ male AGD)	-/-/8.960 for kidney effects (BMDL10) Human equivalent dose (HED): -/-/0.609 Extrapolation to cover uncertainty for other endpoints: -/-/0.1	25 (10 for intraspecies, 2.5 for toxicodynamics and 1 for toxicokinetic, as toxicokinetic intraspecies differences were addressed using HED)	**4** (to be compared with external human dose) **($DNEL_{estro}$ 1)**		EFSA TDI, covers effects on reproduction, mammary development and other effects. See reference for details. DNEL external is applied for comparison with external human exposure

							values.
DTU (Based on Delclos et al., 2014)	Rat	Mammary hyperplasia in adult females	0.025/0.080/- Conversion from rat to human using factor 0.72 (EFSA 2015): 18/57.6/-	25 (10 for intraspecies, 2.5 for toxicodynamics)	**0.7** (to be compared with external human dose) **($DNEL_{estro}$2)**		Based on study by Delclos et al., 2014, and use of assessment factors as in EFSA 2015. DNEL external is applied for comparison with external human exposure values.
Anses 2015/ ECHA 2015 (Moral et al., 2008)	Rats	Mammary development	0.025/0.080/-	300 (10 Interspecies x10 toxicokinetics/toxicodynamics x 3 uncertainty low dose and NMDR)	0.083	0.0025 (3% absorption fraction)	
Comments: Two different DNELs are listed for estrogenic effects of Bisphenol A. **$DNEL_{estro}$1 of 4 µg/kg bw/d** corresponds to the EFSA TDI, and **$DNEL_{estro}$2 of 0.7 µg/kg bw/d** was derived by DTU from a two-generation study showing low-dose effects on mammary gland development (Delclos et al., 2014). Both values are listed in the main report (Table 7.2) and carried forward to risk assessment.							
Bisphenol F							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Stroheker et al. 2003	Female rats, 22 days old, 4 days of exposure by gavage, 0, 25, 50, 100, 200 mg/kg bw/day	↑ relative uterine wet weight at 100 and 200 mg/kg bw/day, ↑ relative uterine dry weight at 200 mg/kg bw/day	50/100/-	100	500	**500 ($DNEL_{estro}$)**	
Higashihara et al. 2007	Adult rats, 28 day oral exposure to 0, 20, 100 and 500 mg/kg bw/day of Bisphenol F, 100% pure. n=10 males and 10 females.	High dose: ↓ T3 and ↑ T4 in males and females. ↑ relative male, but not female, thyroid weight. ↓ body weights (86-87% of controls) and ↑ relative liver weights in males and females. No histological findings in thyroids reported.	100/500/-	100	1000	**1000 ($DNEL_{thyr}$)**	

Comments: **$DNEL_{estro}$ of 500 µg/kg bw/d** was derived from a uterotrophic assay in immature rats (Stroheker et al 2003). This finding is supported by uterotrophic effects in a study using subcutaneous injections in immature rats (Yamasaki et al 2004) and is supported by evidence of estrogenic mode of action in vitro, as reviewed by Rochester et al., 2015. An anti-androgenic effect observed in in vitro studies was not reflected in a Hershberger study in vivo according to Rochester et al., 2015. **$DNEL_{thyr}$ of 1000 µg/kg bw/d** was derived from a study in adult rats (Higashihara et al., 2007). Only few studies on possible endocrine disrupting effects of Bisphenol F are found, and a high degree of uncertainty is associated with these DNELs.

Bisphenol S

Reference	Study design (and exposure route)	Effect-parameter	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELeksternal µg/kg bw/d	DNELinternal µg/kg bw/d	Notes
Yamasaki et al., 2004	Female rats, 20 days old, 3 days of subcutaneous exposure to 20, 100 or 500 mg/kg bw/day of BPS with or without co-exposure to ethinyl estradiol (EE)	↑ absolute and relative uterine wet and blottet weights at high dose. With EE co-exposure, these organ weights were increased at 20 mg/kg and ↓ at 500 mg/kg of BPS.				**500 ($DNEL_{estro}$)**	Indications of estrogenic as well as anti-estrogenic effects depending on dose level and hormonal background. Weak estrogenic effect at high dose, and less marked than seen with lower doses of BPF in the same study. Subcutaneous exposure is not relevant for DNEL derivation for the oral route. However, a parallel study on Bisphenol F showed a comparable effect size at the approximately same doses.

Comments: **$DNEL_{estro}$ of 500 µg/kg bw/d** was derived from a study on BPF using oral dosing of immature female rats (Stroheker et al., 2003; see above), as no study on oral dosing with BPS was found, and as effect sizes for BPS and BPF were comparable at the same doses in a study using subcutaneous exposure of immature rats (Yamasaki et al., 2004). This evidence of estrogenic effect of BPS is supported by evidence of estrogenic mode of action in vitro, as reviewed by Rochester et al., 2015. The data for BPS are not considered to be very robust, and a high degree of uncertainty is associated with this DNEL.

Nonylphenol

Reference	Study design (and exposure route)	Effect-parameter	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELeksternal µg/kg bw/d	DNELinternal µg/kg bw/d	Notes
(NTP 1997)	Rats, two generation study	Changes in oestrous cycle, time of vaginal opening, ovarian weight, sperm/spermatide numbers	15/50/-	2.5*4*10=100	150	**15** (oral absorption factor of 10%) **($DNEL_{estro}$)**	Estrogen in vitro, but also slightly antiandrogenic acc. to 2 in vitro studies. There are several Reproduction studies, but this is used in the EU RAR and has the lowest

							NOAEL below the lowest LOAEL of 2 studies
Comments: **$DNEL_{estro}$ of 15 µg/kg bw/d** was derived from a two-generation study in rats. Data for Nonylphenol, showing endocrine disruptive (estrogenic) effects are considered reliable. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							

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Pesticides

Linuron							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
McIntyre et al. 2000	Pregnant rats, gavage GD 12 to 21. 0, 12.5, 25 or 50 mg/kg bw/day. N=11	Hypoplasia of testes and epididymides, histological changes; few affected at low dose and clear effect at middle dose; nipple retention at high doses	12.5/25/-	100	125	**125 (DNELaa)**	12.5 may be a LOAEL, but only few individuals affected

Wilson et al., 2009	Pregnant rats, Gavage GD 13 to GD 18. 0, 12.5, 25, 50, 75 mg/kg bw/day	↓ testosterone production from 50 mg/kg bw/day	25/50/-	100	250	250	
Comments: **$DNEL_{aa}$ of 125 µg/kg bw/d** was derived from a study on gestational exposure to linuron (McIntyre et al., 2000). Several studies using one dose of linuron show evidence of adverse effects on male reproductive organs. Linuron is AR antagonist and steroid synthesis inhibitor in vitro and inhibits fetal testosterone production in vivo (Wilson et al., 2009).							
Diazinon							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Comments**
EFSA peer review	Rat, two generation study	↓fertility (↓ number of pregnancies), ↑ dystocia (=reduced ability to give birth)	7/35/-	100	70	**70 (DNELaa)**	Reproductive toxicity NOAEL set in peer review report based on reduced fertility.
Comments: **$DNEL_{aa}$ of 70 µg/kg bw/d** was based on the reproductive toxicity NOAEL set by EFSA in peer review report based on reduced fertility. It is not clear whether this effect is directly related to an endocrine mode of action, but diazinon was estrogenic in vitro (Kojima et al., 2005) and has shown effects on sex hormone levels, sperm count and quality in several rodent studies after perinatal (Jayachandra and D'Souza 2014) or adult exposure (ElMazoudy and Attia, 2012). Data for Diazinon showing endocrine disruptive (anti-androgenic) effects are considered robust, but DNEL determination is considered less robust. No indications of thyroid disrupting effects were identified.							
Dithiocarbamates (mancozeb, maneb, probineb)	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
(Stadler et al., 1990)	Rats, two years dietary exposure	↓ T3 and T4, ↑ TSH and thyroid weight, altered thyroid histology	4.8 (125 ppm)/ 28 (750 ppm) / -	2.5*4*10=100	48	**48 (DNELthyr)**	NOAEL for Mancozeb. Used by JMPR for mancozeb and Maneb
Comments: **$DNEL_{thyr}$ of 48 µg/kg bw/d** was based on a 2-year rat study (Stadler et al., 1990) and supported by several other studies showing comparable effects. Data for Dithiocarbamates showing thyroid hormone disrupting effects are considered robust. No data for effects on the reproductive system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
Pirimiphos-methyl							
(Ngoula et al., 2007)	Rats, 90 day study, n=6. 0, 41.67, 62.5	↓ semen quality, histological	62,5/125/-	2.5*4*10=100	625	**625 (DNELaa/estro)**	

	or 125 mg/kg of pirimiphos-methyl	changes in testes					
Comments: **$DNEL_{aa/estro}$ of 625 µg/kg bw/d** was based on data from a 90 day study in rats (Ngoula et al., 2007). Data for Pirimiphos-methyl, showing antiandrogen and estrogenic effects is considered to be reliable and supported by AR antagonist and estrogen effect in vitro (Orton et al., 2011), but the determination of DNEL is considered to be less robust. No data for effects on the thyreoid hormone system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
Procymidone							
(EFSA 2009)	Rats, exposed during pregnancy	↓ AGD, hypospadia, testes effect	ND/2,5/-	2.5*4*10*3*3=900	2,8	**2,8 ($DNEL_{aa}$)**	Extra faktor 3 for "severity of effects"; 0,0028 is new ADI from 2009
Comments: **$DNEL_{aa}$ of 2.8 µg/kg bw/d** was based on reduced AGD , increased incidence of hypospadias and testes effects in rats (EFSA 2009). Data for Procymidone, showing antiandrogenic effects are considered reliable. No data for effects on the thyreoid hormone system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							

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EFSA peer review Diazinon

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UV filtres

BP-3							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
(Schlumpf et al., 2001)	Rats, uterotrophic, dietary exposure	↑ uterine weight in immature rats in the uterotrophic assay	937/1525/-	2.5*4*10=100	9370	**9370 (DNELestro)**	Supported by estrogenic effects in vitro in this and other studies.
Comments: **$DNEL_{estro}$ of 9370 µg/kg bw/d** was derived from a study showing uterotrophic effects in orally exposed immature rats (Schlumpf et al., 2001). Data for benzophenone-3 relative to DNEL determination is considered to be subject to some uncertainty, as other published studies examining lower doses of BP-3showed no effect on the uterine weight (Schlect et al 2004; Suzuki et al 2005). No data for effects on the thyroid hormone system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							
OMC							
Reference	**Study design (and exposure route)**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELeksternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
(Axelstad et al., 2011)	Pregnant rats, GD 7 to PND 17	↓ testosterone levels (male PND16), Progesterone levels (female PND28) and sperm count. At higher doses also ↓ weight of testes and prostate and histological changes in these organs.	ND/500/-	2.5*4*10*3=300	1667	**1667 ($DNEL_{estro}$)**	Estrogenic effect supported by findings of increased uterus weight, altered uterus histology and altered gene expression in uterus in screening studies for estrogenic effects (Sclumpf et al., 2001, Seidlova-Wuttke et al., 2006; Klammer et al., 2005)
(Klammer et al., 2007)	Rats, 5 days gavage	↓ T4	100/333/-	2.5*4*10=100	1000	**1000 ($DNEL_{thyr}$)**	Effect observed after 5 days gavage dosing
Comments: **$DNEL_{estro}$ of 1667 µg/kg bw/d** was derived from a study showing effects on sex hormone levels, sperm count and male reproductive organs in rats, and is supported by findings of an estrogenic mode of action in screening studies for estrogenic effects (Sclumpf et al., 2001, Seidlova-Wuttke et al., 2006; Klammer et al., 2005). **$DNEL_{thyr}$ of 1000 µg/kg bw/d** was derived from a short term study in rats (Klammer et al., 2007), and is supported by other studies showing reductions in T4 levels in rats (e.g. Axelstad et al., 2011). Data for OMC, showing effects plausibly induced through estrogenic and thyroid disrupting modes of action are considered reliable. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).							

References:

Axelstad M, Boberg J, Hougaard KS, Christiansen S, Jacobsen PR, Mandrup KR, Nellemann C, Lund SP, Hass U. Effects of pre- and postnatal exposure to the UV-filter octyl methoxycinnamate (OMC) on the reproductive, auditory and neurological development of rat offspring. Toxicol Appl Pharmacol. 2011 Feb 1;250(3):278-90. doi: 10.1016/j.taap.2010.10.031.

Klammer, H., C. Schlecht, et al. (2007). "Effects of a 5-day treatment with the UV-filter octyl-methoxycinnamate (OMC) on the function of the hypothalamo-pituitary-thyroid function in rats." Toxicology **238**(2-3): 192-199.

Klammer H, Schlecht C, Wutttke W, Jarry H. Multi-organic risk assessment of estrogenic properties of octyl-methoxycinnamate in vivo – a 5-day subacute pharmacodynamic study with ovariectomized rats. Toxicology 2005. 215(1-2):192-199.

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Schlecht C, Klammer H, Jarry H and Wuttke W (2004). Effects of estradiol, benzophenone-2 and benzophenone-3 on the expression pattern of the estrogen receptors (ER) alpha and beta, the estrogen receptor-related receptor I (ERR1) and the aryl hydrocarbon receptor (AhR) in adult ovariectomized rats. Toxicology 205(1-2): 123-130.

Schlumpf, M., B. Cotton, et al. (2001). "In vitro and in vivo estrogenicity of UV screens." Environ.Health Perspect. **109**(3): 239-244.

Seidlova-Wuttke D, Christoffel J, Rimoldi G, Jarry H, Wuttke W. Comparison of effects of estradiol with those of octylmethoxycinnamate and 4-methylbenzylidene camphor on fat tissue, lipids and pituitary hormones. Tox Appl Pharmacol 2006. 214(1):1-7.

Suzuki T, Kitamura S, Khota R, Sugihara K, Fujimoto N, et al. (2005). Estrogenic and antiandrogenic activities of 17 benzophenone derivatives used as UV stabilizers and sunscreens" Toxicology and Applied Pharmacology 203(1): 9-17

Other compounds

Octamethylcyclotetra-siloxane (D4)

Reference	Study design (and exposure route)	Effect-parameter	NOAEL/ LOAEL/ BMDL (mg/kg bw/day)	Assessment factors	DNELeksternal µg/kg bw/d	DNELinternal µg/kg bw/d	Notes
(Siddiqui et al., 2007)	Rats, 2. generation study, inhalation	↓ fertility and ↓ litter size	19.5/32.5/-	2.5*4*10=100	195	**195 (DNELestro)**	NOAEL 300 ppm in inhalation study, conversion to internal dose was based on SCCS 2010

Comments: **$DNEL_{estro}$ of 195 µg/kg bw/d** was derived from a two generation study in rats (Siddiqui et al., 2007). Data for Siloxane D4 showing endocrine disruptive (estrogenic) effects are considered robust**.** An estrogenic mode of action is supported by increased uterus weight and altered serum hormone levels in screening studies for estrgoneic effect in mice (He et al., 2003), and rats (McKim et al., 2001; Quinn et al., 2007). No data for effects on the thyroid hormone system was located. These evaluations are based on detailed data selection in a report by MST 2012 (pregnant consumers).

References:

He B, Rhodes-Brower S, Miller MR, Munson AE, Germolec DR, et al. Octamethylcyclotetrasiloxane exhibits estrogenic activity in mice via ERalpha. Toxicol Appl Pharmacol 2003. 192(3): 254-261.

McKim J M, Wilga PC, Breslin WJ, Plotzke KP, Gallavan RH, et al.. Potential estrogenic and antiestrogenic activity of the cyclic siloxane octamethylcyclotetrasiloxane (D4) and the linear siloxane hexamethyldisiloxane (HMDS) in immature rats using the uterotrophic assay" Toxicological Sciences 2001. 63(1): 37-46.

MST 2012. Gravide forbrugeres udsættelse for mistænkte hormonforstyrrende stoffer. Kortlægning af kemiske stoffer i forbrugerprodukter nr. 117. Miljøstyrelsen.

Quinn AL, Dalu A, Meeker LS, Jean PA, Meeks RG, et al.. Effects of octamethylcyclotetrasiloxane (D-4) on the luteinizing hormone (LH) surge and levels of various reproductive hormones in female Sprague-Dawley rats. Reproductive Toxicology 2007. 23(4): 532-540.

SCCS (2010). Opinion on triclosan (antimicrobial resistance), 22 June 2010.

Siddiqui, W. H., D. G. Stump, et al. (2007). "A two-generation reproductive toxicity study of octarnethylcyclotetrasiloxane (D(4)) in rats exposed by whole-body vapor inhalation." Reproductive Toxicology **23**(2): 202-215.

Appendix 7b

Tables for establishing DNEL values for chronic neurotoxicity

For the derivation of DNEL-values in relation to the neurotoxic effects of the substances the most recent expert assessment of the individual substances (.e.g. opinions from EU-scientific expert groups; reports from EU-working groups, or from national authorities e.g. US EPA and Danish EPA), have been searched. The provided data concerning neurotoxicity in these reports were evaluated in order to identify the most appropriate point of departure data (i.e. NOAEL-, LOAEL- or BMDL-value) for the DNEL derivation. It should be noticed that the DNEL value in relation to the neurotoxic effects may not be the same value as the DNEL (or TDI value) concluded by the expert assessment if e.g. other toxic end-points than neurotoxicity for the substance have resulted in lower DNEL (or TDI level) in the expert assessment.

In the tables below the relevant references used for each substance are given and the dose metric used as point of departure for DNEL derivation is given (i.e. NOAEL, LOAEL or BMDL -values). Further, the use of assessment factors is indicated as used in the reference. If assessment factors have not been applied to the specific dose-metric the methodology as indicated in REACH-guidance R8 is used for the derivation of a DNEL value. Also, if indicated from the reference the *internal DNEL* value is given. Alternatively, the internal DNEL value is estimated if data on the absorption rate for the relevant route of exposure is available.

Bolded values are values that will be used further in this project for the risk assessment of the exposure scenarios.

Acrylamide							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
EFSA 2015	NTP (2012) 2-year study in F344 rats using oral dose levels from 0.33 mg/kg/d to 2.71 mg/kg/d.	Dose related peripheral nerve (sciatic) axonal degeneration	-/-/ 430 as BMDL10 level (o)	12.5 (interspecies factor higher than normal default value due to specific toxicokinetic data) X 10 (intraspecies) Total = 125	**3.4 (o)**		
Comments:							
References: EFSA (2015). EFSA opinion on acrylamide in food. EFSA Journal 2015;13(6):4104.Reffering to: NTP (National Toxicology Program), 2012. NTP Technical Report on the Toxicology and Carcinogenesis Studies of Acrylamide (CAS No. 79-06-1) in F344/N rats and B6C3F1 mice (feed and drinking water studies). NTP TR 575. NIH Publication No. 12-5917. National Institutes of Health. Public Health Service. U.S. Department of Health and Human Services. July 2012.							

Bisphenols; Bisphenol A							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
ECHA/RAC (2015)	Study by Xu et al. (2010). Perinatal oral (intra-gastric) exposure to BPA (GD7-PND21) at doses ranging from 0 – 0.05 – 0.5 – 5 and 50 mg/kg	Brain and behavior, mice. Negative effects on expression of hippocampal NMDA receptors.	**50/500/-**	10 interspecies 10 intraspecies 3 factor for severity for neurotoxicity and uncertainties at the low dose levels	**0.16 µg/kg/d oral**	**0.005** **µg/kg/d** Using an oral absorption factor of 3%	Specific DNEL for neurotoxicity given in the reference. Dermal absorption considered very uncertain: in the range of 10-60%.

	bw/day in mice	Impaired memory. Oral, mice.		Total: 300			

Comments: ECHA/RAC (2015) specifically addressed neurotoxicity as the most critical effect with a **DNELinternal of 0.005 ug(kg bw/d.** The EFSA (2015) opinion was also consulted and here a BMDL10 in relation to effects of kidney weights in mice was defined as the critical end-point and a dose-metric for neurotoxicity was not considered as an adequate starting-point for calculation of a TDI.

ECHA/RAC (2015) also evaluated ***Bisphenol F*** *and* ***Bisphenol S*** and collected data on these substances. However, no data on neurotoxicity is available on these substances and the substances cannot be considered further in the risk assessment in this project.

References:

ECHA/RAC 2015: Committee for Risk Assessment (RAC) and Committee for Socio-economic Analysis (SEAC). Background document to the Opinion on the Annex XV dossier proposing restrictions on 4.4'-isopropylidenediphenol (Bisphenol A; BPA) (reference to Xu XH, Zhang J, Wang YM, Ye YP, and Luo QQ. 2010). Perinatal exposure to bisphenol-A impairs learning-memory by concomitant down-regulation of N-methyl-D-aspartate receptors of hippocampus in male offspring mice. Hormones and Behavior 58 (2): 326-333).
EFSA 2015: Scientific Opinion on the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs. Panel on Food Contact Materials, Enzymes, Flavourings and Processing Aids. EFSA Journal 2015; 13(1):3978

Brominated compounds

HBCDD							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
EFSA 2011	Eriksson et al. 2006. Single oral exposure to mice of 0.9 or 13.5 mg/kg on PND10	Behavioural effects including changes in rearing, locomotion and habituation	-/0.9/0.93 as $BMDL_{10}$ oral dose 0.93 mg/kg in mice corresponding to 0.003 mg/kg/d for humans using toxicokinetic modelling.	2.5 interpsecies, dynamics X 3.2 intraspecies, kinetics = 8	**0.4 oral**		
Comments: EFSA 2011 concluded the behavioural findings in the study of Eriksson as the most critical in relation to adverse effect from HBCDD, however, due to limitations and uncertainties in the current data base, EFSA concluded that it was inappropriate to use the BMDL to establish a health based guidance value and instead used 0.003 mg/kg/d as a human reference dose point and used an overall assessment factor of 8 in order to evaluate the MoE (Margin of Exposure) for the current population exposure.							
References: EFSA (2011a). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Hexabromocyclododecanes (HBCDDs) in Food. EFSA Journal 2011;9(7):2296. [118 pp.] doi:10.2903/j.efsa.2011.2296. Referring to Eriksson P, Fischer C, Wallin M, Jakobsson E and Fredriksson A, 2006. Impaired behaviour, learning and memory, in adult mice neonatally exposed to hexabromocyclododecane (HBCDD). Environmental Toxicology and Pharmacology, 21, 317-322.							

Deca-BDE							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
EFSA 2011	Viberg et al. 2007. Mice single oral exposure to newborn offspring.	Altered total acitvity	-/-/1.70 as BMDL10 1.70 mg/kg in mice corresponds to a human dose at 1.70 mg/kg as no	2.5 Interspecies, dynamics	**680 oral**		

			toxicokinetic modelling is considered necessary for deca-PDE.				

Comments: EFSA 2011 concluded the behavioural findings in the study of Viberg et al. 2007 as the most critical in relation to adverse effect from deca-BDE, however, due to limitations and uncertainties in the current data base, EFSA concluded that it was inappropriate to use the BMDL to establish a health based guidance value and instead used 1.70 mg/kg/d as a human reference dose point and used an overall assessment factor of 2.5 in order to evaluate the MoE for the current population exposure. An uncertainty factor of 2.5 for interspecies differences was considered sufficient as an overall uncertainty factor as no factors in relation to toxicokinetics should be used because of the modelling approach.

Reference:

EFSA (2011). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Journal 2011;9(5):2156. [274 pp.] Reffering to: Viberg H, Fredriksson A and Eriksson P, 2007. Changes in spontaneous behaviour and altered response to nicotine in the adult rat, after neonatal exposure to the brominated flame retardant, decabrominated diphenyl ether (PBDE 209). Neurotoxicology, 28, 136-142.

BDE-47

Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2011	Eriksson et al 2001. Mice single oral exposure to newborn offspring	**Altered locomotion**	-/-/ 0.309 as BMDL10 level in mice corresponding to 172 ng/kg/d in humans using toxicokinetic modelling	2.5 Interspecies, dynamics	**0.07 oral**		

Comments: EFSA 2011 concluded the behavioural findings in the study of Eriksson et al. 2001 as the most critical in relation to adverse effect from BDE-47, however, due to limitations and uncertainties in the current data base, EFSA concluded that it was inappropriate to use the BMDL to establish a health based guidance value and instead used 172 ng/kg/d as a human reference dose point and used an overall assessment factor of 2.5 in order to evaluate the MoE for the current population exposure. An uncertainty factor of 2.5 for interspecies differences was considered sufficient as an overall uncertainty factor as no factors in relation to toxicokinetics should be used because of the modelling approach.

Reference:

EFSA (2011). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Journal 2011;9(5):2156. [274 pp.] Reffering to: Eriksson P, Jakobsson E and Fredriksson A, 2001. Brominated flame retardants: a novel class of developmental neurotoxicants in our environment? Environmental

Health Perspectives, 109, 903-908.

BDE-99							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2011	Viberg et al 2004. Mice single oral exposure to newborn offspring	Altered total acitvity	-/-/ 0.012 as BMDL10 level in mice corresponding to 4.2 ng/kg/d in humans using toxicokinetic modelling	2.5 Interspecies, dynamics	**0.0017 oral**		
Comments: : EFSA 2011 concluded the behavioural findings in the study by Viberg et al. 2004 as the most critical in relation to adverse effect from BDE-99, however, due to limitations and uncertainties in the current data base, EFSA concluded that it was inappropriate to use the BMDL to establish a health based guidance value and instead used 4.2 ng/kg/d as a human reference dose point and used an overall assessment factor of 2.5 in order to evaluate the MoE for the current population exposure. An uncertainty factor of 2.5 for interspecies differences was considered sufficient as an overall uncertainty factor as no factors in relation to toxicokinetics should be used because of the modelling approach.						
Reference: EFSA (2011). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Journal 2011;9(5):2156. [274 pp.] Reffering to : Viberg H, Fredriksson A and Eriksson P, 2004. Neonatal exposure to the brominated flame-retardant, 2,2',4,4',5-pentabromodiphenyl ether, decreases cholinergic nicotinic receptors in hippocampus and affects spontaneous behaviour in the adult mouse. Environmental Toxicology and Pharmacology, 17, 61-65.						

BDE-153							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (mg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2011	Viberg et al. 2003. Mice single oral exposure to newborn offspring	Altered total acitvity	-/-/ 0.083 as BMDL10 level in mice corresponding to 9.6 ng/kg/d in humans using toxicokinetic	2.5 Interspecies, dynamics	**0.0038 oral**		

			modelling				

Comments: : EFSA 2011 concluded the behavioural findings in the study by Viberg et al. 2001 as the most critical in relation to adverse effect from BDE-153, however, due to limitations and uncertainties in the current data base, EFSA concluded that it was inappropriate to use the BMDL to establish a health based guidance value and instead used 9.6 ng/kg/d as a human reference dose point and used an overall assessment factor of 2.5 in order to evaluate the MoE for the current population exposure. An uncertainty factor of 2.5 for interspecies differences was considered sufficient as an overall uncertainty factor as no factors in relation to toxicokinetics should be used because of the modelling approach.

Reference:

EFSA (2011). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Polybrominated Diphenyl Ethers (PBDEs) in Food. EFSA Journal 2011;9(5):2156. [274 pp.] Reffering to : Viberg H, Fredriksson A and Eriksson P, 2003. Neonatal exposure to polybrominated diphenyl ether (PBDE 153) disrupts spontaneous behaviour, impairs learning and memory, and decreases hippocampal cholinergic receptors in adult mice. Toxicology and Applied Pharmacology, 192, 95- 106.

TBBPA							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
EFSA 2011	EFSA (2011) concluded that from the limited available studies, exposure to TBBPA during development does not appear to induce relevant neurobehavioural changes.						

Comments: Not further included for quantitative risk assessment, however, some studies indicating neurobehavioural changes may indicate concern regarding neurotoxicity.

References:

EFSA (2011b). EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Tetrabromobisphenol A (TBBPA) and its derivatives in food. EFSA Journal

Chlorinated compounds

PCBs, total							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (µg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
Danish EPA 2014	ATSDR (2000) referring to Rice (1999). Monkeys orally exposed from birth to 20 week of age to 7.5 µg/kg/d PCB-mixture resembling the PCB-content in human milk	Neurobehavioural changes	-/7.5/-	2.5 (interspecies) x 2 (allometric interspecies) x 10 (intraspecies) x 3 (LOAEL to NOAEL) = 150 (assessment factors specifically applied for this project)	**0.05 oral**	**0.05 (assuming 100% oral absorption)**	
Comments: The calculated **DNELinternal of 0.05 µg/kg bw/d** is in relation to a PCB mixture as this occur when taken up in the human food chain, thus it covers both dioxin-like and non-dioxin like PCBs. Danish EPA (2014) indicates that it is not possible to make DNEL specifically for non-dioxinlike PCBs as a separate group. As exposure to PCB in food always is to a mixture of dioxin + non-dioxinlike PCB congeners the DNEL as indicated would seem more relevant than a DNEL for non-dioxin-like PCB in isolation.							
References: Danish EPA (2014). Evaluation of health hazards by exposure to Polychlorinated biphenyls (PCB) and proposal of a health-based quality criterion for soil. Environmental Project No. 1485, 2014 (refence to ATSDR (2000). Toxicological Profile for Polychlorinated Biphenyls (Update). U.S. Department of Health & Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry. Rice. D. C. (1999). Behavioral impairment produced by low-level postnatal PCB exposure in monkeys. Environ. Res. 80: 113-121).							

PCBs, dioxin-like and dioxins							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (µg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
SCF 2001	Faqi et al. (1998). Subcutaneous injections of 25 ng*/kg bw in rat	Changes in sexual behaviour of male rat offspring + decreased	-/20 pg*/kg/d /- The animal dose estimated to be	3.2 (intraspecies) x 3 (LOAEL to NOAEL)		**2 pg*/kg/d**	***TCDD equivalents

	offspring.	sperm counts.	equivalent to 20 pg/kg/d /for humans considering differences in kinetics.	= 10			

Comments: The TDI or **DNEL of 2 pg TCDD eqv/kg/d** as calculated by SCF (2001) is both in relation to neurotoxic effects as well as to reproductive toxicity.

References:

SCF (Scientific Committee on Food) (2001). Opinion on the risk assessment of dioxins and dioxins-like PCBs in food (update based on the new scientific information available since the adoption of the SCF opinion of 22 November 2000) (adopted by the SCF on 30 May 2001) http://europa.eu.int/comm/food/fs/sc/scf/out90_en.pdf. (Reference to Faqi, A.S., Dalsenter, P.R., Merker, H.-J., and Chahoud, I. (1998). Reproductive toxicity and tissue concentrations of low doses of 2,3,7,8-tetrachlorodibenzo-p-dioxin in male offspring rats exposed throughout pregnancy and lactation. Toxicol. Appl. Pharmacol., 150, 383-392).

Trichloroethylphosphate (TCEP)

Reference	Study; design and exposure route	Effect-parameter	NOAEL/ LOAEL/ BMDL (µg/kg bw/day)	Assessment factors	DNELexternal µg/kg bw/d	DNELinternal µg/kg bw/d	Notes
EU RAR	NTP 103-week (gavage) rat study. F344/N using doses of 0; 44 and 88 mg/kg/d 5d/week	degenerative lesions in the brain	44000/ 88000/- X 5d/7d = 31500/63000	10 (interspeices) 10 (intraspecies)	**315 (o)**		Oral absorption in rats was concluded to be > 90% i.e. oral exposure is approximately comparable to internal exposure

Comments:

References:

EU-RAR (2009). European Union Risk Assessment Report on TRIS (2-CHLOROETHYL) PHOSPHATE, TCEP, July 2009, p 1-213. With reference to:
NTP (1991). National Toxicology Program: Technical report series No. 391. "Toxicology and carcinogeneses studies of tris(2-chloroethyl)phosphate (CAS No. 115-96-8) in F344/N rats and B6C3F1 mice (gavage studies)", US Department of Health and Human Services.

Fluorinated compounds

PFOA							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
US EPA 2016a	Neurotoxicity not discussed as a possible critical end-point for PFOA by US EPA. Few data in neurotoxicity of PFOA was described. Onishchenko et al. (2011) in a non-guideline study exposed mice orally during the whole gestation period to 0.3 mg/kg/d. Behavioral changes in male and female offspring were observed in this study.						
EFSA 2008	Neurotoxicity not identified as a critical end-point for PFOA by EFSA						
Comments: The referred study by US EPA indicates a neurotoxic potential comparable to the effects found for PFOS. DNEL for PFOS of **0.03 µg/kg/d should apply for PFOA** as well.							
References: EFSA, 2008. Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts. Scientific Opinion of the Panel on Contaminants in the Food chain. The EFSA Journal (2008) 653, 1-131 US EPA, 2016a. Health Effects Support Document for Perfluorooctanoic Acid (PFOA). U.S. Environmental Protection Agency. EPA 822-R-16-003. May 2016. (Reference to Onishchenko, N., C Fischer, W.N.W. Ibrahim, S. Negri, S. Spulbur, S. Cottica, and S. Ceccatelli. 2011. Prenatal exposure to PFOS or PFOA alters motor function in mice in a sex-related manner. Neurotoxicity Research 19:452–461).							

PFOS							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
US EPA 2016b	Butterhoff et al.(2009). An OECD 426 study with rats.	Increased motor activity and impaired habituation in offspring.	0.3/1 /- 0.3 mg/kg/d in rats equivalent to a human intake of 0.84 µg/kg/d considering the differences in kinetics.	3 (interspecies toxicodynamic) x 10 (intraspecies)	**0.03 oral**	**0.03 µg/kg/d** **(assuming 100 oral absorption)**	The neurotoxic effects indentified as one of several cirtical effects of PFOS by US EPA
Comments: EFSA 2008 was also consulted, however, neurotoxicity was not identified as a critical end-point for PFOS by EFSA. A **DNELinternal of 0.03 µg/kg/d for neurotoxicity** is							

concluded as calculated by US EPA.

References:

EFSA, 2008. Perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and their salts. Scientific Opinion of the Panel on Contaminants in the Food chain. The EFSA Journal (2008) 653, 1-131
US EPA, 2016b. Health Effects Support Document for Perfluorooctane Sulfonate (PFOS). U.S. Environmental Protection Agency.: EPA 822-R-16-002. May 2016. (Reference to: Butenhoff, J.L., D.J. Ehresman, S.-C. Chang, G.A. Parker, and D.G. Stump. 2009. Gestational and lactational exposure to potassium perfluorooctane-sulfonate (K+PFOS) in rats: Developmental neurotoxicity. Reproductive Toxicology 27:319–330).

PFHxS							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
NCM 2013 **Livsmedesverket 2013**	These reviews did not find any data in relation to neurotoxicity. Critical effects were considered to be reproduction and liver toxicity.						
Comments: No further evaluated for neurotocxicity.							
References: Livsmedelsverket (2013). Riskvärdering av perfluorerande alkylsyror i livsmedel och dricksvatten. Rapport 11-2013. NCM (2013). Per- and polyfluorinated substances in the Nordic Countries - Use, occurence and toxicology. TemaNord 2013:542							

Hydrocarbons/ solvents

Hydrocarbons + tetrachloroehtylene							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(mg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
Danish EPA 2016	The following **DNEL values (mg/m^3) for inhalation** specifically for chronic neurotoxicity for children below 3 years were derived in the report: n-hexane 0.700 n-heptane - Toluene 0.725 Xylenes 0.125 Ethylbenzene 0.200 Styrene 0.175 Methylstyrene 0.200 Propylbenzenes 0.240 Trimethylbenzenes 0.100 Diisopropylbenzene 0.200 Phenyloctane 0.275 C7-C12 hydrocarbons, total 1.425 Tetrachloroethylene 1.650 For details regarding NOAL/LOAEL identification and estimation of DNEL values using assessment factors according to the REACH ECHA guidance the Danish EPA (2016) report should be consulted.						

Comments: In the Danish EPA 2016 report the starting point for the assessment of the substances was the report*"Harmonisation framework for health based evaluation of indoor emissions from construction products in the European Union using the EU-LCI concept"* from Joint Research Centre/ EU-Commission (JRC/EU-Commission 2013) where tolerable exposure levels for most of the hydrocarbons were derived in order to protect against chronic neurotoxic effects.
When calculating the tolerable exposure levels, the fact that children in relation to their bodyweight inhale larger volumes of air than adults is taken into account, and also an additional uncertainty factor of 2 is used to take into account children's increased sensitivity regarding effects on the central nervous system. For details please consult the Danish EPA (2016) report: http://www2.mst.dk/Udgiv/publications/2016/02/978-87-93435-42-1.pdf.

Reference:

Danish EPA 2016).Survey and risk assessment of toluene and other neurotoxic substances in children's rooms. Survey of chemical substances in consumer products No. 145, 2016. Danish Environmental Protection Agency.

Metallic compounds

Aluminium							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
JECFA 2012 **SCCS 2014**	Poirier et al. (2011). 12 months oral neuro-developmental toxicity study in rats at dose levels of 30,100 and 300 mg Al/kg/d	reduced grip strength and increased foot splay	30 000/100 000/-	10 (interspecies) x 10 (intraspecies) = 100 (applied by JECFA)	**300 (o)**	**0.3 (int)**	Oral bioavailability of 0.1%
Comments: With respect to neurotoxicity SCCS 2014 concluded: "There are suggestions that persons with some genetic variants may absorb more aluminium than others, but there is a need for more analytical research to determine whether aluminium from various sources has a significant causal association with Alzheimer disease and other neurodegenerative diseases. Both EFSA and JECFA concluded that the information available was inconsistent and did not support a causal association between aluminium exposure and Alzheimer's disease or other chronic neurological diseases. Aluminium is a neurotoxicant in experimental animals. However, most of the animal studies performed have several limitations and therefore cannot be used for quantitative risk assessment. In conclusion, SCCS considers that Aluminium (Al) is a known neurotoxicant and circumstantial evidence has linked this metal with several neurodegenerative disorders like Alzheimer's disease, Parkinson's diseasesand other chronic neurodegenerative diseases but no causal relationship has yet been proven." However, SCCS 2014 agreed on NOAEL 30 mg/kg bw/d used by JECFA for risk assessment. JECFA established a Provisional Tolerable Weekly Intake (PTWI) of 2 mg/kg bw (corresponding to 0.3 mg/kg/d as indicated above) based on a neuro-developmental toxicity study of aluminium citrate administered via drinking water to rats.							
References: JECFA (2012). Safety evaluation of certain food additives and contaminants: Prepared by the seventy-fourth meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series. 65: 3-86. SCCS (2014). OPINION ON the safety of aluminium in cosmetic products Scientific Committee on Consumer Safety. SCCS/1525/14 Revision of 18 June 2014. With reference to: Poirier J, Semple H, Davies J, Lapointe R, Dziwenka M, Hiltz M and Mujibi D. (2011). Double-blind, vehicle-controlled randomized twelve-month neurodevelopmental toxicity study of common aluminium salts in the rat. Neuroscience. 193: 338-362.							

Lead							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
ECHA /RAC 2014 **EFSA 2010**	EFSA (2010) assessed a series of epidemiological studies relating blood-lead levels and IQ loss in children. Further, EFSA (2010) modelled the relation between blood lead levels and daily exposure levels. I.e. a human dose response was established between intake levels and IQ loss.	IQ loss in children	-/-/0.5 as BMDL01 level for oral exposure. **No threshold** for the neurotoxic effects of lead in humans has been identified. Exposure at the BMDL01 value corresponds to an IQ loss of 1 IQ point in children.	10	**0.05 (o) as a DMEL value with "no appreciable risk for children"**		
Comments: ECHA/RAC (2014) used an assessment factor of 10 for going from the BMDL01 level to a DMEL level of "no apprecialbe risk for children"							
References: ECHA/ RAC (2014). Background document to the Opinion on the Annex XV dossier proposing restrictions on Lead and its compounds in articles intended for consumer use. ECHA/RAC/RES-O-0000003487-67-04/F; ECHA/SEAC/ RES-O-0000003487-67-05/F. EFSA (2010), Scientific Opinion on Lead in Food. EFSA Panel on Contaminants in the Food Chain (CONTAM EFSA Journal 2010; 8(4):1570							

Mercury as inorganic mercury							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (µg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2012	Huang et al. (2011) exposed mice to mercuric chloride by oral gavage at 0.37 mg/kg b.w. per day, expressed as mercury 4 weeks before mating and the offspring up til 21 days postnatally.	Ototoxicity ; behavirourl changes	-/370/-	17.5 (interspecies, from mice) x 10 (interspecies) x 3 (LOAEL to no-effect) = 525	**0.70 (o)**		
Comments: EFSA (2012) used data on kidney toxicity as most critical end-point for their TDI derivation for inorganic mercury (a TDI of 0.57 µg/kg/d) as data on these effects were considered more robust and also occurred at lower levels than the neurotoxic effects. Thus the DNEL derived above is specifically derived for this project and in relation to neurotoxicity.							
References: EFSA (2012). Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal 2012;10(12):2985. With reference to: Huang CF, Liu SH, Hsu CJ and Lin-Shiau SY, 2011. Neurotoxicological effects of low-dose methylmercury and mercuric chloride in developing offspring mice. Toxicology Letters, 201, 196-204.							

Mercury as methylmercury							
Reference	**Study; design and exposure route**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL (µg/kg bw/day)**	**Assessment factors**	**DNELexternal µg/kg bw/d**	**DNELinternal µg/kg bw/d**	**Notes**
EFSA 2012	EFSA (2012) chose a maternal hair content of mercury of 11.5 mg/kg as an apparent NOEL in	Impaired performance in neurobehavioural testing	A mercury content if 11.5 mg/kg in hair was estimated by EFSA to be associated to a daily	2 (data derived variation factor) x 3.2 (intraspecies toxicokinetic	**0.19 (o)**		

	connection with methylmercury ingesting for the basis for derivation of a health-based guidance value. This value was chosen based on the data from the epidemiological studies from the Seychelles nutrition cohort and from the Faroese Cohort.		methylmercury intake of 1.2 µg/kg/d (expressed as Hg)	factor) = 6.4			
Comments:							
References: EFSA (2012). Scientific Opinion on the risk for public health related to the presence of mercury and methylmercury in food. EFSA Journal 2012;10(12):2985							

Pesticides

Pesticides							
Reference	**Substances**	**Effect-parameter**	**NOAEL/ LOAEL/ BMDL** **(µg/kg bw/day)**	**Assessment factors**	**DNELexternal** **µg/kg bw/d**	**DNELinternal** **µg/kg bw/d**	**Notes**
Jensen et al. 2015	*Organophosphates* Diazinon Dimethoate Chlorfenvinphos Methamidophos Oxydemeton-methyl *Carbamates* Carbaryl Benomyl Methomyl	Regarding acetylcholine esterase inhibition there has been some debate as to whether to include carbamates and organophosphates in a common assessment group. The argument for having a common assessment group including both carbamates and organophosphates was that there is a potential for concurrent exposure to substances from both groups from various sources in the diet (DTU Food 2014). Therefore organophosphates and carbamates are in the context of this report grouped together due to the common mechanism of action as acetylcholineesterase inhibitors The ADI values derived by EFSA, JMPR or the EU Commission may be based on other effects than neurotoxicity, however, in the context of this report the ADI values considering all types of effects are also considered to be protective against the neurotoxicity of the substances.			**0,2 (o)** **1,0 (o)** **0,5 (o)** **1,0 (o)** **0,3 (o)** **7,5 (o)** **20 (o)** **2,5 (o)**		
Comments: If exposure with the use of the present ADI values indicate concern it may be necessary to further examine the background data for the ADI value, as other effects responsible for the ADI value may have occurred at lower levels than neurotoxic effects. Thus a DNEL specifically for neurotoxic effects would in these cases most probably be higher than the indicated ADI value.							
References: DTU Food (2014). Identification of Cumulative Assessment Groups of Pesticides. EXTERNAL SCIENTIFIC REPORT submitted to EFSA. *Jensen BH, Petersen A, Nielsen E, Christensen T, Poulsen ME, Andersen JH. Cumulative dietary exposure of the population of Denmark to pesticides. Food Chem Toxicol. 2015 Sep; 83: 300-7.*							

Appendix 8

Tables for estimations of RCR-values

Table 8A. Antiandrogenic substances, RCRaa for children below 3 years of age calculated from sum of exposures from consumer products, indoor environment and foods. RCRaa is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for antiandrogenic substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	*DNELaa (µg/kg lgv/dag)*	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)
Chlorinated compounds					
PCBs/dioxins	0.000002	2.12E-06	4.6E-06	*1.06*	*2.3*
PCBs/dioxins (indoor)	0.033	0	0.3	0	*9.09*
Perfluorinated compounds					
PFOS	0.08	0.00141	0.00378	0.0176	0.0473
Phthalates					
DEHP	35	12.37	56.26	*0.353*	*1.607*
DBP	6.7	2.18	11.93	*0.325*	*1.787*
DiBP	8.3	2.36	18.77	*0.284*	*2.26*
BBP	500	0.39	2.85	0.00078	0.0057
DiNP	1500	2.3	9.1	0.00153	0.00607
Di-n-hexyl phthalate	500	0	0	0	0
DCHP	180	0.106	0.383	0.000589	0.00213
Dipentyl phthalate	330	0	0	0	0
Medicines					
Paracetamol	500	12500	50000	*25*	*100*
Pesticides					
Linurone	125	0.024	0.024	0.000192	0.000192
Pirimiphosmethyl	625	0.1	0.1	0.00016	0.00016
Procymidone	2.8	0.043	0.043	0.0154	0.0154
SUM (including paracetamol)				**27**	**117**
SUM (without paracetamol)				**2.1**	**17**

Table 8B. Estrogenic compounds, RCRestro for children below 3 years of age calculated from sum of exposures from consumer products, indoor environment and foods. RCRestro is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for estrogenic substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	*DNELestro (µg/kg lgv/dag)*	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)
Parabens					
Butyl- and propylparaben	20	19	59	*0.95*	*2.95*
Phenols					
Bisphenol A	4	0.387	1.108	0.0968	*0.277*
Bisphenol A*	0.7	0.387	1.108	0.55	*1.58*
Bisphenol F	500	0.0223	0.0703	4.46E-05	0.000141
Bisphenol S	500	0.0043	0.0047	8.6E-06	9.4E-06
Nonylphenol	15	0.79	1.975	0.0527	*0.132*
Pesticides					
Diazinon	70	0.011	0.011	0.000157	0.000157
UV-filtres					
BP-3	9370	1700	3300	*0.181*	*0.352*
OMC	1667	1400	2800	*0.840*	*1.68*
Other					
Triclosan	750	7.7	30	0.01	0.04
Siloxane D4	195	0	0	0	0
SUM				**1.8**	**4.8**

Table 8C. Thyroid hormone disrupting compounds, RCRthyr for children below 3 years of age calculated from sum of exposures from consumer products, indoor environment and foods. RCRthyr is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for thyroid hormone disrupting substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	*DNELthyr (µg/kg lgv/dag)*	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)
Antioxidants					
BHA	1000	230.6	571	*0.231*	*0.572*
BHT	250	111	383	*0.44*	*1.5*
Brominated compounds					
DecaBDE	2.7	0.0105	0.098	0.00389	0.0363
HBCDD	41	0.007	0.3327	0.000171	0.00812
TBBPA	160	0	0.0603	0	0.000377
Chlorinated compounds					
PCBs/dioxins	0.000006	2.12E-06	4.6E-06	*0.353*	*0.767*
Perfluorinated compounds					
PFOA	20	0.00364	0.00567	0.000182	0.000284
PFOS	0.1	0.00141	0.00378	0.0141	0.0378
PFHxS	17	0.00016	0.00024	9.41E-06	1.41E-05
Phthalates					
DEHP	263	12.37	56.26	0.0470	0.214
DCHP	900	0.106	0.383	0.000118	0.000426
Di-n-hexyl phthalate	6100	0	0	0	0
DnOP	368	0.04	0.35	0.000109	0.000951
DPHP	100	0.1	0.26	0.001	0.0026
Phenols					
Bisphenol F	1000	0.0223	0.0703	2.23E-05	7.03E-05
Pesticides					
Dithiocarbamates	48	0.5	0.5	0.0104	0.0104
UV-filtres					
OMC	1000	1400	2800	*1.4*	*2.8*
Other					
Triclosan	30	7.7	30	*0.26*	*1*
SUM				**2.7**	**6.7**

Table 8D. Antiandrogenic compounds, RCRaa for the pregnant woman/unborn child calculated from sum of exposures from consumer products, indoor environment and foods. RCRaa is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for antiandrogenic substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	*DNELaa (µg/kg lgv/dag)*	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)
Chlorinated compounds					
PCBs/dioxins	0.000002	1.06E-06	2.3E-06	*0.53*	*1.15*
PCBs/dioxins (indoor)	0.033	0	0.2	0	*6.06*
Perfluorinated compounds					
PFOS	0.08	0.000468	0.068	0.00585	0.85
Phthalates					
DEHP	35	4.09	13.01	*0.117*	*0.371*
DBP	6.7	0.84	2.93	*0.125*	*0.437*
DiBP	8.3	0.81	2.73	0.0976	0.329
BBP	500	0.25	0.83	0.0005	0.00166
DiNP	1500	0.467	2.2	0.000311	0.00147
Di-n-hexyl phthalate	500	0	0	0	0
DCHP	180	0.016	0.031	8.89E-05	0.00017
Dipentyl phthalate	330	0	0	0	0
Medicines					
Paracetamol	500	16670	66670	*33.3*	*133.3*
Pesticides					
Linurone	125	0.012	0.018	0.000096	0.000144
Pirimiphosmethyl	625	0.05	0.079	0.00008	0.000126
Procymidone	2.8	0.021	0.033	0.0075	0.0118
SUM (including paracetamol)				**34.2**	**142.6**
SUM (without paracetamol)				**0.9**	**8.4**

Table 8E. Estrogenic compounds, RCRestro for the pregnant woman/unborn child calculated from sum of exposures from consumer products, indoor environment and foods. RCRestro is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for estrogenic substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	*DNELø (µg/kg lgv/dag)*	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)
Parabens					
Butyl- and propylparaben	20	3.8	16	*0.19*	*0.8*
Phenols					
Bisphenol A	4	0.216	1.066	0.054	*0.267*
Bisphenol A*	0.7	0.216	1.066	*0.31*	*1.52*
Bisphenol F	500	0.0075	0.0197	0.000015	3.94E-05
Bisphenol S	500	0.0013	0.0017	2.6E-06	3.4E-06
Nonylphenol	15	5.0377	10.1857	*0.336*	*0.679*
Pesticides					
Diazinon	70	0.0055	0.0086	7.86E-05	0.000123
UV-filtres					
BP-3	9370	720	1400	*0.077*	*0.149*
OMC	1667	600	1200	*0.361*	*0.720*
Other					
Triclosan	750	7.3015	22	0.00974	0.0293
Siloxane D4	195	10.2	200	0.0523	*0.11*
SUM				**1.1**	**2.8**

Table 8F. Thyroid hormone disrupting compounds, RCRthyr for the pregnant woman/unborn child calculated from sum of exposures from consumer products, indoor environment and foods. RCRthyr is calculated for scenarios with middle and high exposures. SUM indicates the RCRtotal for thyroid hormone disrupting substances. RCR values above 0.1 for single compounds are marked in italics.

Substance	***DNELthyr (µg/kg lgv/dag)***	**Sum (mean exposure)**	**Sum (high exposure)**	**RCR (mean exposure)**	**RCR (high exposure)**
Antioxidants					
BHA	1000	130	1140	*0.13*	*1.14*
BHT	250	42	260	*0.168*	*1,04*
Brominated compounds					
DecaBDE	2.7	0.003	0.005	0.00111	0.00185
HBCDD	41	0.0002	0.0008	4.88E-06	1.95E-05
TBBPA	160	0	0.0026	0	1.63E-05
Chlorinated compounds					
PCBs/dioxins	0.000006	1.06E-06	2.3E-06	*0.177*	*0.383*
Perfluorinated compounds					
PFOA	20	0.00059	0.000944	2.95E-05	4.72E-05
PFOS	0.1	0.000468	0.068	0.00468	0.68
PFHxS	17	0.00003	0.00005	1.76E-06	2.94E-06
Phthalates					
DEHP	263	4.09	13.01	0.0156	0.0495
DCHP	900	0.016	0.031	1.78E-05	3.44E-05
Di-n-hexyl phthalate	6100	0	0	0	0
DnOP	368	0.022	0.063	5.98E-05	0.000171
DPHP	100	0	0	0	0
Phenols					
Bisphenol F	1000	0.0075	0.0197	7.5E-06	1.97E-05
Pesticides					
Dithiocarbamates	48	0.24	0.39	0.005	0.00813
UV-filtres					
OMC	1000	600	1200	*0.6*	*1.2*
Other					
Triclosan	30	7.3015	22	*0.243*	*0.733*
SUM				**1.3**	**4.6**

Table 8G. RCR values for neurotoxic substances, children below 3 years

Susbstance	DNEL (µg/kg lgv/dag)	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)	RCR (specific worst case)
Brominated substances						
HBCDD	0,40	0.0070	0.3327	0.0175	0.8318	
Deca-BD	680	0.0105	0.0980	0.0000	0.0001	
Penta-BDE-47	0.07	0.0180	0.0700	0.2571	1.0000	
Penta-BDE-99	0.0017	0.0070	0.0260	4.1176	15.2941	
Chlorinated substances						
Total PCB(6)	0.05	0.0126	0.0386	0.2520	0.7720	
PCB, dioxinlike + dioxins	2.00	2.1000	4.6000	1.0500	2.3000	
Tetrachlorethylen	1650	3.0000	100.0000	0.0018	0.0606	
TCEP	440	13.7100	18.5000	0.0312	0.0420	
Fluorinated substances						
PFOA	0.03	0.0036	0.0057	0.1213	0.1890	
PFOA, worst case	0.03		0.0140			0.4667
PFOS	0.03	0.0014	0.0038	0.0470	0.1260	
PFOS, worst case	0.03		0.0130			0.4333
Hydrocarbons (µg/m^3)						
Toluene	725	9.10	55.3	0.0126	0.0763	
Toluene, worst case	725		230			0.3172
Xylenes	125	7.50	42.3	0.0600	0.3384	
Xylenes, worst case	125		146			1.1680
Ethylbenzene	200	3.20	8.20	0.0160	0.0410	
Ethylbenzene, worst case	200		230			1.1500
C7-C12-hydrocarbons, total	1425	79	232	0.0554	0.1628	
C7-C12-hydrocarbons, worst case indoors	1425		1500			1.0526

Styrene	175		2.50		0.0143	
Metals						
Aluminium	0.30	0.1360	0.2860	0.4533	0.9533	
Lead	0.05	2.5600	11.56	51.20	231	
Mercury, inorganic	0.70	0.1900	0.31	0.2714	0.4429	
Mercury, inorganic, worst case (damaged light bulb)	0.70		10.0			14.3
Methylmercury	0.19	0.0390	0.2300	0.2053	1.2105	
Pesticides *(only mean exposure estimates available)*						
Diazinon	0.20	0.0110		0.0550		
Dimethoate	1.00	0.0150		0.0150		
Chlorfenvinphos	0.50	0.0066		0.0132		
Methamidophos	1.00	0.0069		0.0069		
Oxydemeton-methyl	0.30	0.0018		0.0060		
Carbaryl	7.50	0.1000		0.0133		
Carbendazim and benomyl	20.00	0.2000		0.0100		
Methomyl and thiodicarb	2.50	0.0200		0.0080		
Phenols						
Bisphenol A	0.160		0.387		0.8780	2.4188
Bisphenol A. worst case (pacifier)	0.16			0.2300		
Other substances						
Acrylamid	3.40	1.40	2.40	0.4118	0.7059	
SUM				**61**	**261**	

Table 8H. RCR values for neurotoxic substances, pregnant woman/ unborn child.

Substance	DNEL (µg/kg lgv/dag)	Sum (mean exposure)	Sum (high exposure)	RCR (mean exposure)	RCR (high exposure)	RCR (specific worst case)
Brominted substances						
HBCDD	0.40	0.0002	0.0008	0.0005	0.0020	
Deca-BDE	680	0.0030	0.0050	0.0000	0.0000	
Penta-BDE-47	0.07	0.0020	0.0070	0.0286	0.1000	
Penta-BDE-99	0.0017	0.0007	0.0014	0.4118	0.8235	
Chlorinated substances						
Total PCB(6)	0.05	0.0063	0.0118	0.126	0.236	
PCB, dioxinlike + dioxins	2.00	1.06	2.30	0.530	1.150	
Tetrachlorethylene	1650	3.00	100	0.0018	0.0606	
Tetrachlorethylene, worst case	1650	-	767	-		0.4648
TCEP	440	-	4.5	-	0.0102	
TCEP worst case (baby sling)	440		72.5			0.16
Fluorinated substances						
PFOA	0.03	0.0006	0.0009	0.0197	0.0315	
PFOA, worst case	0.03	-	0.0061	-		0.2039
PFOS	0.03	0.0005	0.0012	0.0156	0.0413	
PFOS, worst case	0.03	-	0.0068	-		0.2267
Hydrocarbons (µg/m^3)						
Toluene	725	9.10	55.3	0.0126	0.0763	
Toluene, worst case	725	-	230	-		0.3172
Xylenes	125	7.50	42.3	0.0600	0.3384	
Xylenes, worst case	125	-	146	-		1.1680
Ethylbenzene	200	3.20	8.2	0.0160	0.0410	
Ethylbenzene, worst case	200	-	230	-		1.1500

C7-C12 hydrocarbons, total	1425	79.0000	232	0.0554	0.1628	
C7-C12 hydrocarbons, total, worst case, indoors	1425		1500			1.05
C7-C12 hydrocarbons, total, worst case, painting indoors	1425		6000000			4210
Styrene	175		2.50		0.0143	
Metals						
Aluminium	0.30	0.041	0.096	0.1367	0.320	
Aluminium, cosmetics	0.30	4.500	85.7	15.0		285
Lead	0.05	0.240	0.840	4.800	16.80	
Mercury, inorganic	0.70	0.026	0.077	0.0371	0.110	
Mercury, inorganic, worst case (damaged light bulb)	0.70		0.280			0.4
Methylmercury	0.19	0.018	0.051	0.0947	0.268	
Pesticids						
Diazinon	0.20	0.0055	0.0086	0.0275	0.0430	
Dimethoate	1.00	0.0073	0.0120	0.0073	0.0120	
Chlorfenvinphos	0.50	0.0033	0.0052	0.0066	0.0104	
Methamidophos	1.00	0.0034	0.0053	0.0034	0.0053	
Oxydemeton-methyl	0.30	0.0009	0.0014	0.0029	0.0047	
Carbaryl	7.50	0.0500	0.0790	0.0067	0.0105	
Carbendazim and benomy.	20.00	0.1000	0.1600	0.0050	0.0080	
Methomyl and thiodicarb.	2.50	0.0100	0.0150	0.0040	0.0060	
Phenols						
Bisphenol A	0.160	0.2160	1.0660	1.3500	6.6625	
Bisphenol A. worst case (thermal paper)	0.005*		0.2600			52
Other substances						
Acrylamid	3.40	0.50	1.00	0.1471	0.2941	0.50
SUM				**7.9**	**27.6**	

Exposure of children and unborn children to selected chemical substances

The overall objective of this project is to assess whether there may be a risk of the overall exposure of children under 3 years and pregnant women/ unborn children to endocrine disrupting substances (including suspected endocrine disrupting substances) and chronic neurotoxic substances. Overall, 37 substances were included regarding endocrine disrupting effects and 39 substances regarding chronic neurotoxic effects, with some overlap (7 substances) between the groups. One can mainly be exposed to the substances investigated via food, drinking water, indoor climate (dust), outdoor environment (soil) and consumer products (cosmetics, toys, chemical products, etc.).

The report has looked at the intrinsic properties of the substances and assessed the risk in relation to the calculated exposure. The risk associated with simultaneous exposure to several substances with the same mode of action is also assessed. The calculations indicate that the overall exposure of children under 3 years and unborn (pregnant women) to endocrine disruptors can cause concern even at average exposures, especially when one considers that a large number of other endocrine disruptors are not included in these calculations. It is generally considered not to be a risk with the use of single products but as previous studies has shown one can be concerned about exposure to some chemicals with the same mode of action.

Although most calculations are made based on a number of assumptions the results of the project is considered to give an indication of which substances on the basis of present knowledge is regarded the most critical in terms of increased risk of endocrine disrupting and neurotoxic effects in children under 3 years and unborn (pregnant).

Environmental
Protection Agency
Strandgade 29
DK-1401 København K

www.mst.dk